UNIT 18

ALDEHYDES AND KETONS

Structure

18.1 INTRODUCTION

In previous units, you have studied the chemistry of alcohols and phenols ethers. In this unit, we deal with aldehydes and ketones. Both these classes of organic compounds have a carbonyl group, >C=O. A ketone has two alkyl (or aryl) or one alkyl and one aryl groups attached to the carbonyl carbon, while an aldehyde has at least one hydrogen atom attached to the carbonyl carbon. The other group in an aldehyde can be alkyl or aryl.

The remarkable reactivity of the carbonyl group makes the chemistry of aldehydes and ketones the backbone of synthetic organic chemistry. The double bond between the carbon and oxygen atoms in these compounds serves as a model for the reaction of many other functional groups containing π bonds between dissimilar atoms. Although the reactions of carbonyl compounds are quite simple, their synthetic utility is enormous. Addition and substitution reactions are of major interest. In this unit, you will learn the basic principles which are responsible for the extreme reactivity of these compounds and on the basis of which reliable predictions can be made.

Here, we will first consider the preparation of aldehydes and ketones and then the characteristic reactions of the carbonyl-group. Finally, we will study industrial uses of aldehydes and ketones and the methods used for their detection. Aromatic aldehydes and ketones unlike aryl halides and phenols do not much differ from aliphatic aldehydes and ketones, you will study them in the next unit.

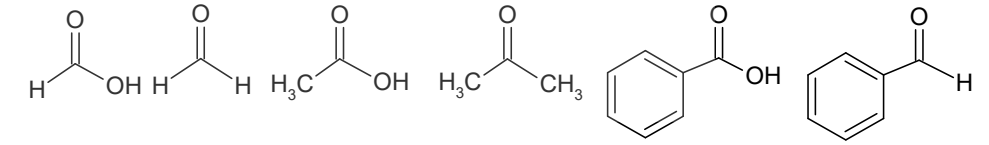
Expected Learning Outcomes

After studying this unit, you should be able to:

- explain the nucleophilic addition reactions of aldehydes and ketones on the basis of the structure of carbonyl group;
- describe the physical properties of aldehydes and ketones;
- list and discuss the preparation of aldehydes and ketones;
- describe the commercial methods of preparation of methanol, ethanol and propanone;
- explain the relative reactivity of aldehydes and ketones;
- describe the reactions of aldehydes and ketones;
- discuss the lab detection of carbonyl compounds and the test which distinguishes aldehydes from ketones; and
- state the industrial uses of aldehyde and ketones.

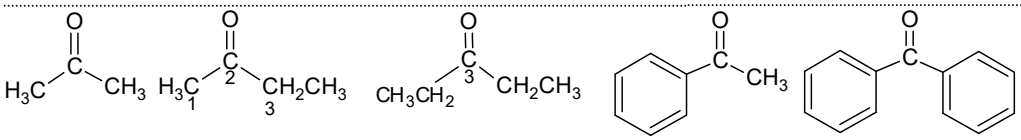
18.2 STRUCTURE AND PHYSICAL PROPERTIES

Before going in details of the chemistry of aldehydes and ketons, let us recall the nomenclature pattern of these compounds. The common names of aldehydes are derived from the common name of the corresponding carboxylic acid, with the ending **-ic** or **-oic** acid replaced by -aldehyde. In the IUPAC system, aldehydes are treated as derivatives of the alkanes, with ending **-e** replaced by **-al**. Thus, an alkane becomes an alkanal. Cyclic and aromatic aldehydes are named as cyclic alkane- or aryl-substituted carbaldehydes. In the examples given below, common names are written in parenthesis.



(Formic acid) Methanal (Formaldehyde) (Acetic acid) Ethanal Acetaldehyde) (Benzoic acid) Benzenecarbaldehyde (Benzaldehyde)

In the IUPAC system, ketones are called **alkanones**, the ending **-e** of the alkane replaced with **-one**. On the other hand, aromatic ketones are named as aryl-substituted alkanones. To indicate the position of carbonyl group in chain, the parent chain is numbered from the direction that gives the carbonyl carbon the smaller number regardless of the presence of substituents or the halogens, hydroxyl, C=C or C≡C functional groups. Cyclic ketones are simply called cycloalkanones and aromatic ketones are named as aryl-substituted alkanone.

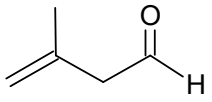


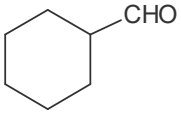
Propanone (Acetone) | 2-Butanone (Ethyl methyl ketone) | 3-Pentanone (Diethyl ketone) | 1-Phenylethanone (Acetophenone) | Diphenylmethanone (Benzophenone)

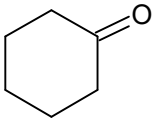
The IUPAC system still retains the common names for formaldehyde, acetaldehyde, bezaldehyde, acetone and benzophenone.

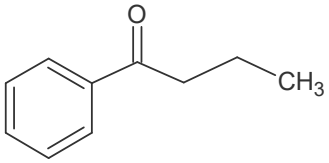
SAQ 1

Name of the following compounds:

a) 

b) 

c) 

d) 

18.2.1 Structure of the Carbonyl Group

In order to understand the chemistry of the carbonyl group, there is a need to look in to details of the structure of the carbonyl group. According to valence bond theory, the carbon-oxygen double bond consists of one σ bond formed by the overlap of sp^2 hybrid orbitals of carbon and oxygen and one π bond formed by the overlap of parallel 2*p* orbitals. The two nonbonding pairs of electrons (unshared electrons pairs) on oxygen lie in the remaining sp^2 hybrid orbitals of oxygen. The sp^2 hybridisation means that the carbonyl group has to be planar, and the angle between the substituent is close to 120°. Fig. 18.1 illustrates all these features for the methanal (CH_2O) molecule. You can notice that the orbital arrangements are somewhat similar to carbon-carbon double bond of alkenes. But when we compare electronic arrangement, we can notice two important differences. First, oxygen atom of carbonyl group bears two nonbonding pairs of electrons located in two sp^2 hybrid orbitals.

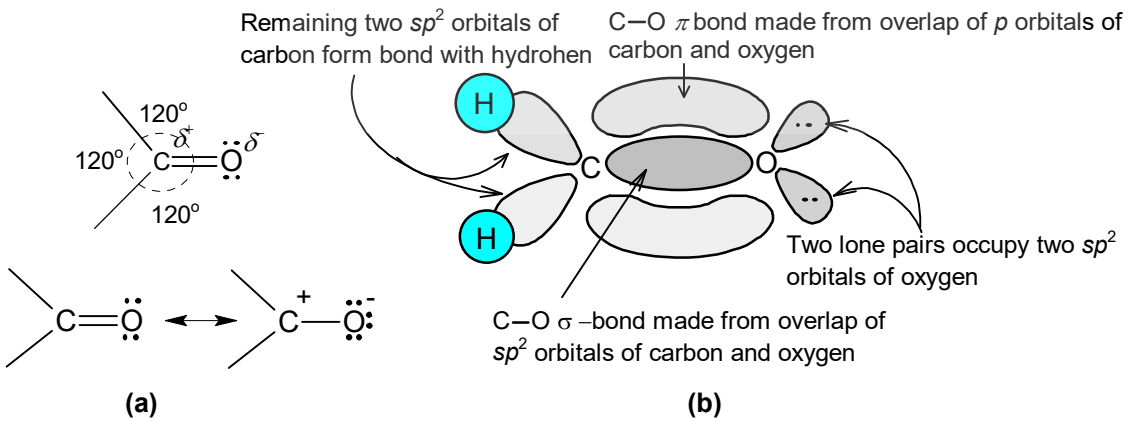
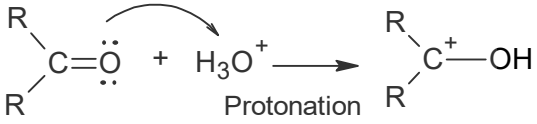


Fig.18.1: (a) Molecular structure of carbonyl group, (b) Orbital picture of methanal.

Second, carbonyl group oxygen is more electronegative than carbon [electronegativity of oxygen on the Pauling Scale = 3.44 and electronegativity of carbon on the Pauling Scale = 2.55]. Therefore, similar to ether group carbon-oxygen double bond is polar with oxygen bearing a partial negative charge and carbon bearing a partial positive charge. These two factors contribute to the high reactivity of the carbonyl group.

In addition, the resonance structures shown in Fig. 18.1(a) emphasise that carbon is an electrophilic site (electron deficient centre) and the oxygen is a nucleophilic site (electron rich centre). Thus, we can say that the carbonyl carbon acts as a Lewis acid and the carbonyl oxygen acts as a Lewis base. As a result, carbonyl carbon is susceptible to attack by a nucleophile. The electrophilicity of carbon centre is further enhanced when reaction is carried out in acidic medium due to the protonation of oxygen atom.



Now, we will apply molecular orbital approach to further understand the chemistry of the carbonyl group. A good approximation for reactivity can be found by looking at the frontier molecular orbitals [highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO)]. In case of carbonyl group, π and π^* are the HOMO and LUMO, respectively. Fig. 18.2 shows, how π and π^* orbitals are formed on mixing of two *p* atomic orbitals of carbon and oxygen.

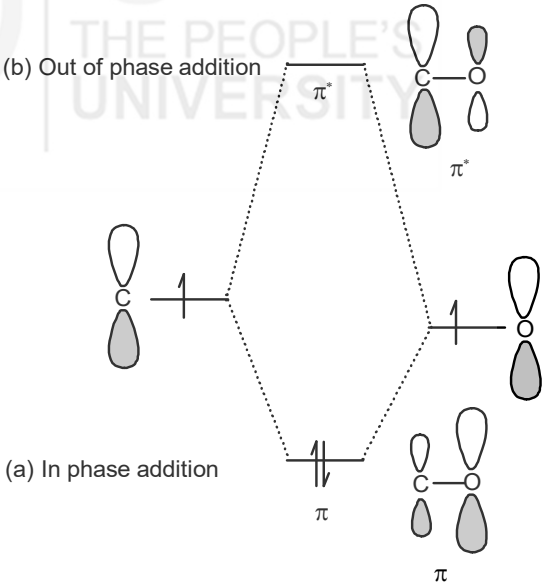


Fig. 18.2: Molecular mixing diagram for the creation of *π* bond in carbonyl group: (a) HOMO and (b) LUMO.

In the above diagram you can notice that *p* orbital of oxygen is lower in energy because oxygen is more electronegative than carbon. According to MO theory, when the two combining atomic orbitals are not equal in energy, the resulting molecular orbitals have a greater contribution from the atomic orbital that is closest in energy. Thus, the bonding π orbital has larger contribution from the oxygen, therefore has larger coefficient at the oxygen atom, and conversely, the anti-bonding π^* orbital has a larger contribution from the

carbon. Further, only the bonding orbital is occupied, the electron density in the bond is concentrated on oxygen. The resultant bond is said to be polarised. Polarisation of the bond means that there is an uneven distribution of electron density between the two combining atoms leading to the buildup of positive charge on the carbon and negative charge on the oxygen and of the carbonyl bond.

Conversely, unfilled antibonding π^* orbital, is polarised in the opposite direction, with larger coefficient at the carbon atom. Thus, when the carbonyl group reacts with a nucleophile, electrons move from the HOMO of the nucleophile into the LUMO of the electrophile, in other words π^* orbital of the carbonyl bond. The greater coefficient of the π^* orbital at carbon means a better HOMO-LUMO interaction. It can be concluded that larger coefficient on oxygen in the filled (bonding) orbital explains why the oxygen atom acts as Lewis base (nucleophilic centre). The larger coefficient on carbon in the empty antibonding, π^* orbital explains why it behaves as a Lewis acid (electrophilic centre).

It can now be summarised that all the concepts discussed above lead to the same conclusion, that is, in aldehydes and ketones, the carbon of carbonyl group is an electrophilic site and oxygen is a nucleophilic site. Thus, because of these structural features, these compounds undergo a wide variety of reactions with most involving nucleopholic addition.

The Angle of Nuecleophilic Attack

When a nucleophile (Nu^-) approaches the carbon atom, the electron pair in its HOMO starts to interact with the LUMO (antibonding, π^*) to form a new σ bond. This interaction leads to breaking of the π bond, leaving only the C–O, σ bond intact. The nucleophilic addition to carbonyl group can be illustrated as follows:

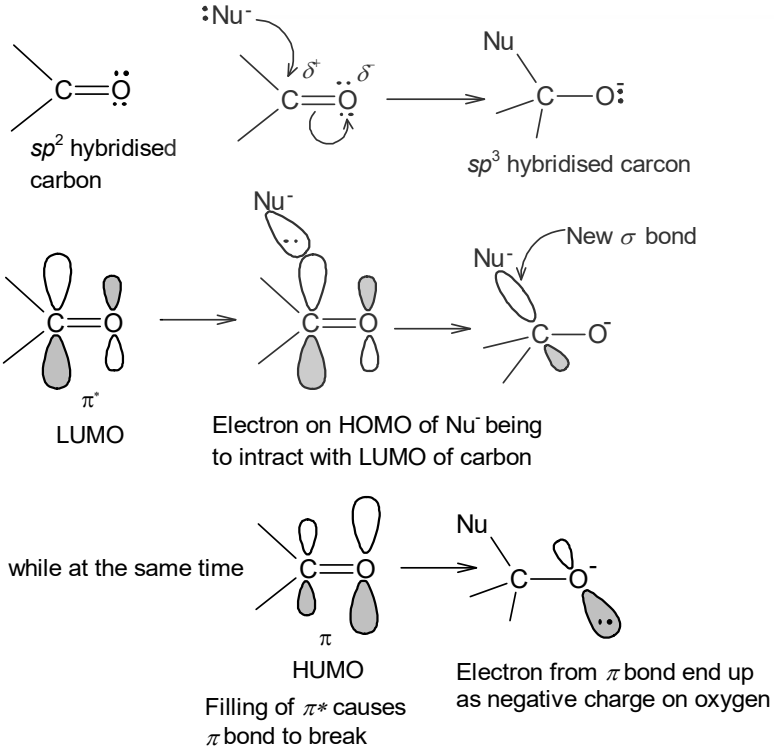
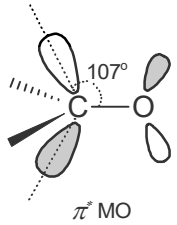


Fig. 18.3: Orbital interaction during nucleophilic attack.

Fig. 18.3 shows how the trigonal, planar sp^2 hybridised carbon atom of the carbonyl group changes to a tetrahedral sp^3 hybridised state in the product. Molecular orbital calculations also suggested that HOMO of the nucleophile approaches from a particular angle; that is, 107° to the plane of the carbonyl group. This approach route is known as the Burgi-Dunitz trajectory.

Burgi and Dunitz deduced this trajectory by examining crystal structures of compounds containing both a nucleophilic nitrogen atom an electrophilic carbonyl group.

The possible explanation for this angle of attack is that due to repulsion of the HOMO by the electron density in the carbonyl π bond, the lobs of LUMO, π^* are already at an angle as shown below.



Burgi-Dunitz angle

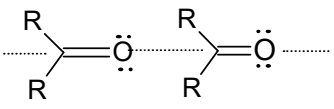
Any other portion of the molecule, that gets in the way of the Burgi-Dunitz trajectory, will greatly reduce the rate of nucleophilic addition to carbonyl group and this is the one of the reasons why aldehydes react faster than ketones in the nucleophillic reactions.

18.2.2 Physical Properties

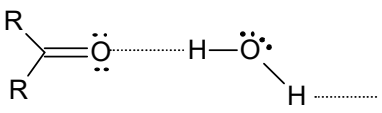
The bond dipole moment of a carbonyl group is 2.3 D

As we have mentioned above, the aldehydes and ketones are polar compounds due to presence of carbonyl group and these compounds possess intermolecular dipole-dipole attraction. Due to these interactions, molecules have higher boiling points than nonpolar compounds of similar molecular weight. The boiling points of aldehydes and ketones are, however, much lower than the boiling points of the corresponding alcohols. This is due to the fact that the molecules of aldehydes and ketones are held together by the much weaker electrostatic interaction between dipoles whereas alcohols are held together by strong hydrogen bonds.

The partial solubility and the formation of hydrates can be explained by the formation of hydrogen bonds between carbonyl compounds and water. The unshared electron pairs on oxygen are responsible for such hydrogen bonding. The carbonyl-carbonyl and carbonyl-water interactions are illustrated in the following structures:



Dipole-dipole intraction between the molecules of carbonyl compounds



Hydrogen bonding between carbonyl compound and water

As the hydrophobic hydrocarbon part of the molecule increases in size, water solubility decreases. The physical properties of some aldehydes and ketones are summarized in Table 18.2.

Table 18.2: Physical properties of some aldehydes and ketones

Aldehydes		Structure Formula	BP, K	Solubility in H_2O
IUAPC	**Common Name**			
Methanal	Formaldehyde	HCHO	252	miscible
Ethanal	Acetaldehyde	CH_3CHO	293	miscible
Propanal	Propionaldehyde	CH_3CH_2CHO	322	16 g/100 cm^3
Butanal	Butyraldehyde	$CH_3CH_2CH_2CHO$	349	7 g/100 cm^3
Benzaldehyde	Benzaldehyde	C_6H_5CHO	451	slightly
Ketones:				
Propanone	Acetone	CH_3COCH_3	329	miscible
2-Butanone	Methy ethyl ketone	$CH_3COCH_2CH_3$	353	26 g/100 cm^3
Phenylethanone	Acetophenone	$C_6H_5COCH_3$	475	insoluble
Diphenyl methanone	Benzophenone	$C_6H_5COC_6H_5$	579	insoluble

SAQ 2

Without consulting Tables given for physical properties of organic compounds, identify which compound in each pair would have the higher boiling point.

a) 1-Pentanal or 1-pentanol

b) 3-Methyl-2-butanone or 2-methylbutane

c) 2-Pentanone or 2-pentanol

d) Cyclohexanone or cyclohexane

e) Pentane or 1-pentanal

18.3 PREPARATION

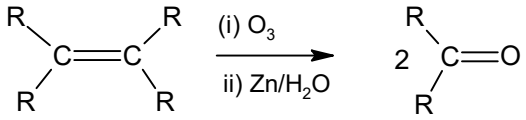
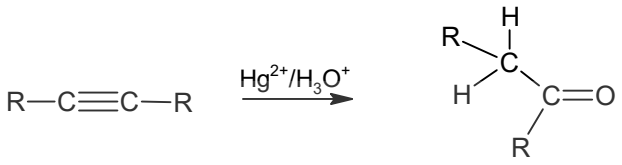
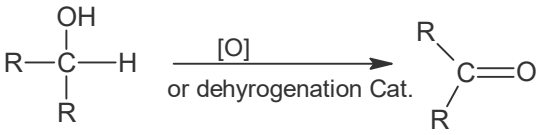
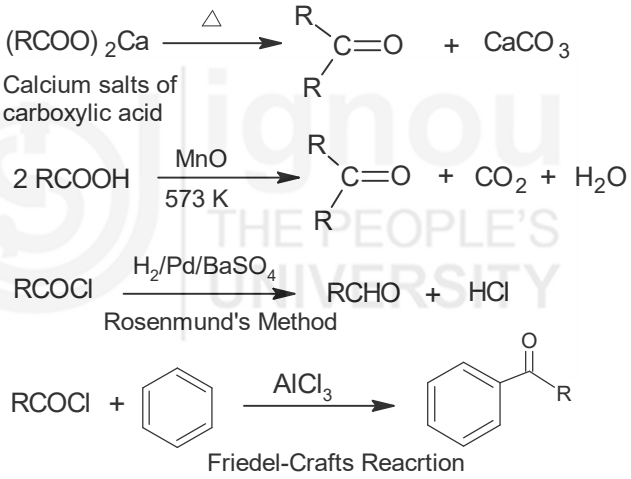
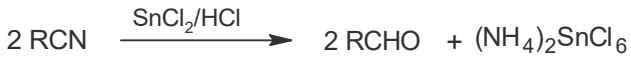
We have already learned several reactions that can be used for the preparation of aldehydes and ketones. Recall the oxidation of alkenes with ozone, hydration of alkynes and oxidation or dehydrogenation of alcohols.

In this section, we will first consider the general methods for the preparation of aliphatic aldehydes and ketones and then follow them up with industrial methods for the production of methanal, ethanal and propanone.

18.3.1 General Methods of Preparation of Aldehydes and Ketones

Aldehydes and ketones can be prepared from alkenes, alkynes, alcohols, carboxylic acids and their derivatives. We are summarising the general reactions of these methods of preparation in Table 18.3.

Table 18.3: Preparation of Aldehydes and Ketones

From Alkenes: Ozonolysis of alkenes

From Alkynes: hydration of alkynes

From Alcohols

From Carboxylic Acids and their Derivatives

From the Stephen's Method


The preparation of aldehydes and ketones from alkenes and alkynes has been discussed in Unit 7 and Unit 8, respectively. Here, we will consider preparation of these compounds from alcohols, and carboxylic acids and their derivatives.

i) From Alcohols

As mentioned in Unit 12, primary alcohols give aldehydes and secondary alcohols give ketones on dehydrogenation/oxidation. The tertiary alcohols are resistant to dehydrogenation/oxidation because the carbon bearing the –OH group is already bonded to three carbon and, therefore, cannot form any additional carbon-oxygen bond. This is the most common way of synthesising aldehydes and ketones in the laboratory. We generally use the following oxidising agents for the oxidation of alcohols:

i) alkaline potassium permanganate solution

ii) hot, concentrated HNO_3

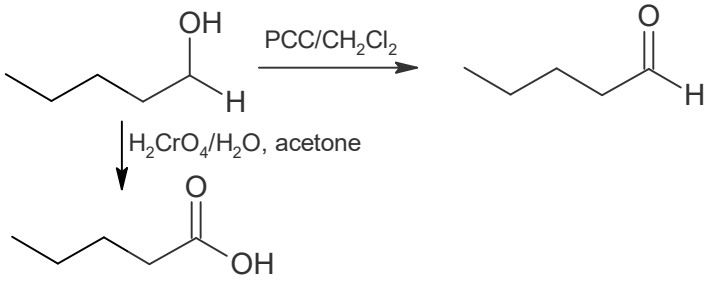
iii) chromic acid (H_2CrO_4)

iv) chromium trioxide (CrO_3) complex with pyridine or with pyridine and HCl (PDC and PCC)

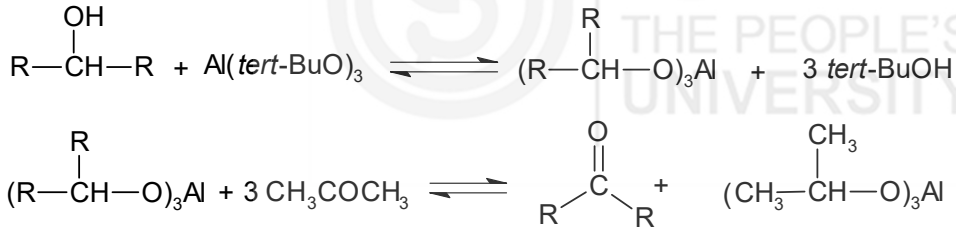
A solution of chromic acid in aqueous sulphuric acid is known as the **Jones reagent**. This reagent is used to distinguish between aldehydes and ketones. Aldehydes give a positive test, but ketones do not. Primary and secondary alcohols also give positive test with Jones reagent but tertiary alcohols do not.

This regent is also selective and does not oxidise alkene and alkyne units if present in same molecule.

The first three methods generally lead to over oxidation of primary alcohols to carboxylic acids. The chromium trioxide complex is most commonly used for oxidation of a primary alcohol to an aldehyde. This reagent is prepared by dissolving CrO_3 in aqueous HCl and adding pyridine to precipitate pyridinium chlorochromate (PCC) as solid. PCC oxidation is carried out in aprotic solvent such as dichloromethane.



Another reagent used for oxidation of secondary alcohols is alumimium tertiary-butoxide. It is used in the **Oppenauer oxidation**. In this method, the reaction mixture is first heated and then propanone (acetone) is added:

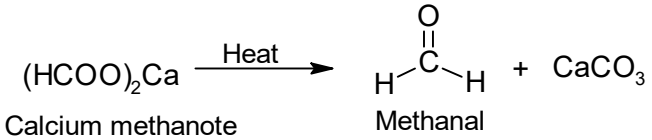


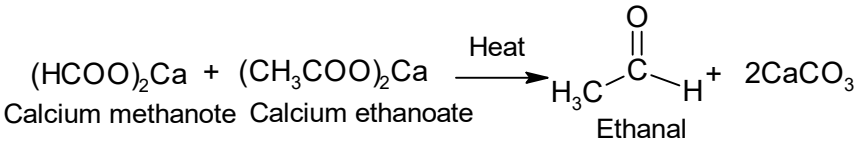
Oppenaure oxidation is reversible and the reverse reaction is known as the Meerwein-Ponndorf-Varley reduction.

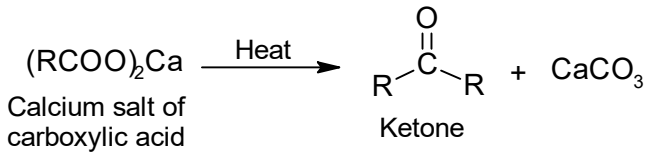
ii) From Carboxylic Acids and their Derivatives

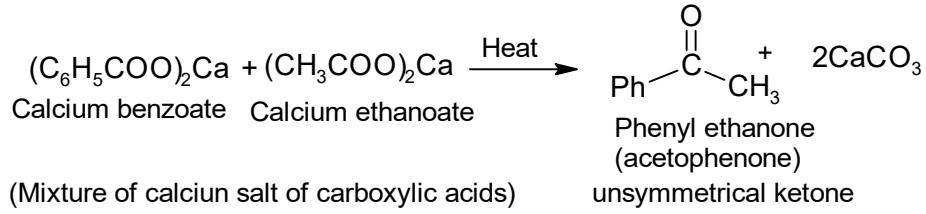
Carboxylic acids can be converted into aldehydes and ketones either by heating their calcium salts or by passing vapours of the acid over heated manganous oxide or by reduction of acid chlorides with hydrogen in the presence of palladium over barium sulphate **(Rosenmund's method)**. We will consider these reactions in more detail in third semester course. General equations for these reactions are given below:

From Calcium Salts of Carboxylic Acids

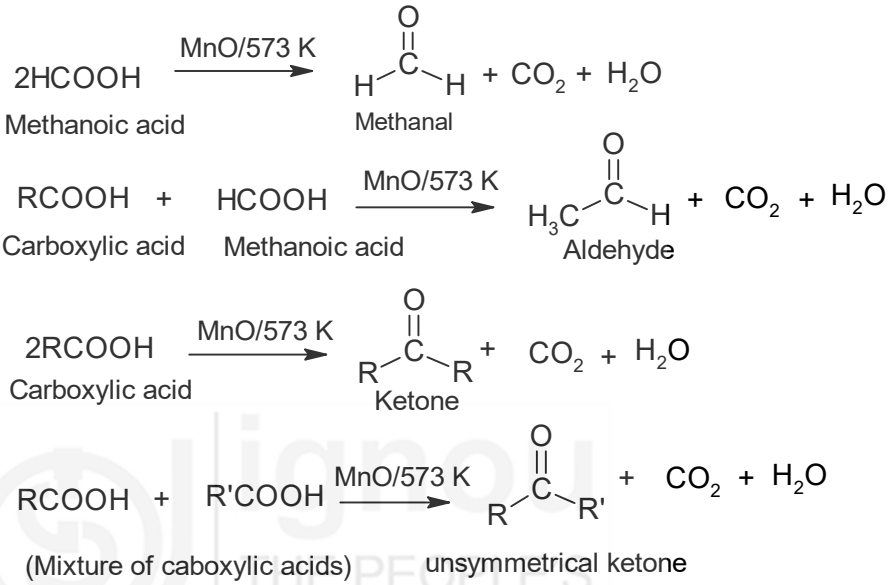






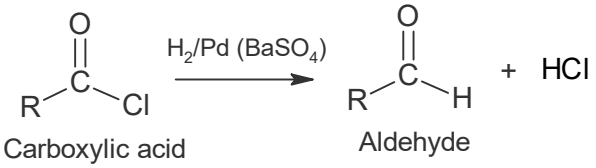


From the Reaction of Carboxylic Acids with Manganese(II) oxide



Please note that for aldehydes other than methanal and for unsymmetrical ketones, a mixture of acids and their calcium salts in molar proportion is taken.

From Acid Chlorides by the Rosenmund's Method

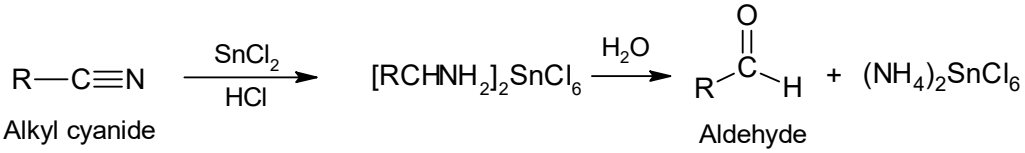


where R = CH_3 or C_6H_5

$BaSO_4$ poisons the catalyst and helps to stop the reduction at the aldehydes stage.

iii) From the Stephen's Method

Reduction of an alkyl cyanide with stannous chloride and hydrochloric acid followed by hydrolysis with steam gives aldehydes **(Stephen's method)**:



where R = CH_3 or C_6H_5

SAQ 3

An organic compound A (molecular formula C_3H_7Cl) was treated with aqueous sodium hydroxide and the vapours of the product obtained were passed over heated copper to give propanone (acetone). A is

a) 1-chloropropane b) 2-chloropropane c) chlorocylclopropane

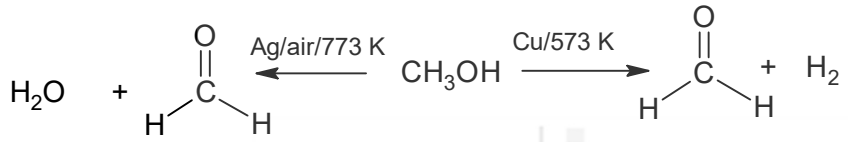
18.3.2 Industrial Methods of Preparation of Aldehydes and Ketones

The industrial preparation of some common carbonyl compounds are described below:

Methanal

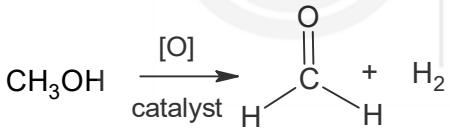
It is manufactured from methanol by following two processes:

i) Oxidation of methanol using silver or copper catalyst.

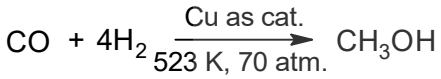


Although the silver catalyst is expensive no silver is lost and catalyst is easily regenerated and can be recycled.

ii) Oxidation using zinc-chromium or iron-molybdenum oxide catalyst.



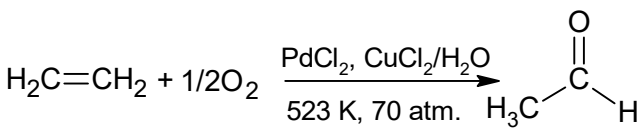
Methanol itself is made from enriched water gas.



Ethanal

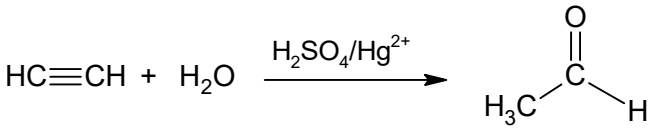
The following methods can be used for the manufacture of ethanol:

i) By passing a mixture of ethene and oxygen under pressure over palladium (II)/Cupric chloride catalyst in water at 323 K, ethanal is produced:

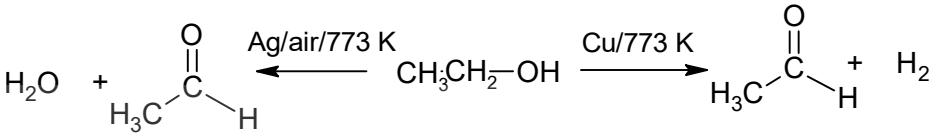


This process is called **Wacker process**. Since ethene is cheaper than ethyne, this process has superseded the two older routes outlined below:

ii) By passing ethyne through dilute sulphuric acid, with mercury(II) sulphate as catalyst at 336 K.

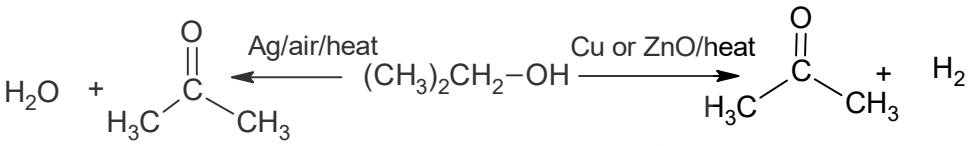


iii) By the oxidation of ethanol (which is manufactured from ethene) in the gas phase over a silver or copper catalyst:

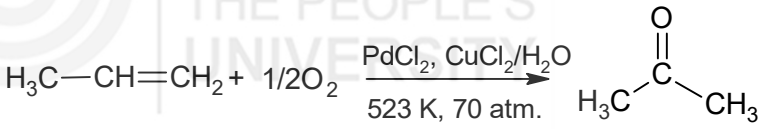


Propanone

Dehydrogenation of 2-propanol over heated copper or zinc oxide or air oxidation over heated silver gives propanone. 2-Propanol is obtained from propene.



Propanone can also be manufactured by the direct oxidation of propene from natural gas with oxygen or air, catalysed by a mixture of palladium and cuprous chlorides (**The Wacker Process**).



We have already seen in Unit 16 that propanone is obtained as a by-product in the oxidation of cumene to phenol.

SAQ 4

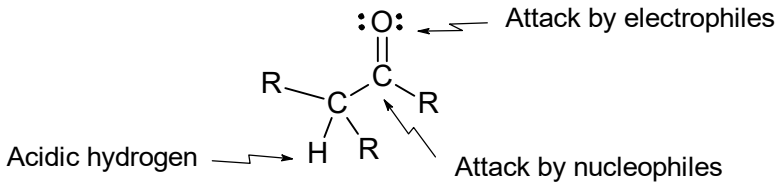
How will you convert propene to acetone?

18.4 REACTIONS OF ALDEHYDES AND KETONES

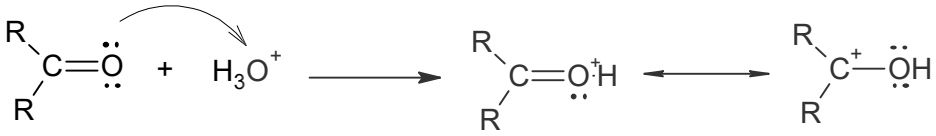
We can group together the reactions of aldehyde and ketones into four categories (a) reactions of the carbonyl group, (b) reactions of the 'α' hydrogen (acidic hydrogen) attached to the carbon adjacent carbonyl group, (c) oxidation reactions and (d) reduction reactions.

As stated earlier, the carbon-oxygen double bond is polar which leads to ionic addition to the carbonyl π bond. A carbonyl compound may first be attacked either by a nucleophile or by an electrophile. Therefore, with most reagents, carbonyl additions show the same overall course, i.e., addition of the negative,

nucleophilic part of the reagent to the carbon atom and addition of the positive electrophilic part to the oxygen atom.

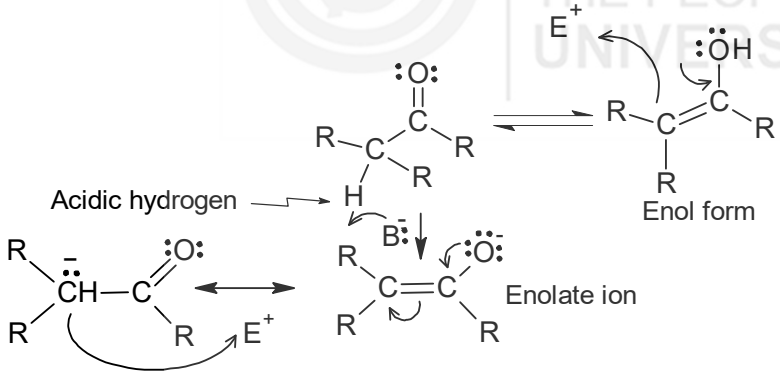


In acidic medium, the proton first adds to the carbonyl oxygen. This further increases the electrophilic nature of the carbonyl carbon.



Resonance structures of protonated carbonyl group

Hence, nucleophilic additions to the carbonyl compounds are very often catalysed by acids. We turn now our attention on the nature of *α* hydrogen atoms attached to carbon next to carbonyl group. The carbonyl group induces enhanced acidity of these hydrogens. Moving or removing these *α* hydrogens may lead to either of two electron-rich species: enols or enolate ions. Both enol and enolate ion behave as nucleophiles and are capable of attacking electrophilic species such as protons, halogens and even carbon centre of carbonyl compounds. A brief description of the reactions due to *α* hydrogen is included in this unit.

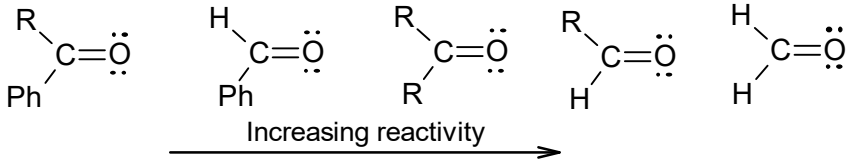


Before going into details of the reactions of carbonyl compounds, let us study the relative reactivity of aldehydes and ketones.

The relative reactivity of aldehydes and ketones in addition reactions may be attributed partly to the extent of polarisation on the carbonyl carbon. The more polarised the carbonyl group the greater the positive charge on the carbonyl carbon. A greater positive charge means higher reactivity. If this partial positive charge is dispersed throughout the molecule, then the carbonyl compound is less reactive.

As you already know the alkyl group is electron releasing (+*I* effect). Therefore, in ketones, due to the presence of two alkyl groups, the carbon of the carbonyl group will be less electron deficient than in aldehydes. Hence, ketones will be less reactive than aldehydes. Further, methanal with no alkyl

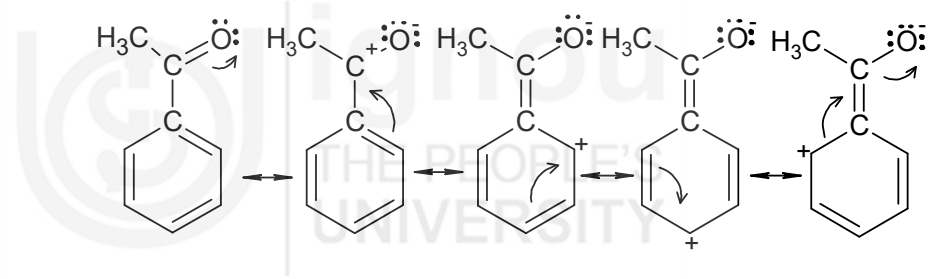
groups attached to the carbonyl carbon is more reactive than ethanal and other susbstituted aldehydes.



The most reactive aldehyde is trichloroethanal (chloral), Cl_3CCHO, in which electron withdrawal by the three chlorine atoms depletes the electrons density on the carbonyl carbon so much that it forms stable hydrates.

Steric factors also play a role in the relative reactivity of aldehydes and ketones. Since hybridisation of the carbonyl carbon changes from sp^2 in the starting material to sp^3 in the addition product, ketones are less reactive than aldehydes because of the un-favourable steric interaction between the two alkyl groups and the other two groups in the product. Lack of such steric hindrance in the product is another reason for the higher reactivity of methanal.

A carbonyl group attached to an aromatic ring is less reactive in addition reactions than it is in aliphatic aldehydes and ketones. This can be attributed to resonance interaction in between the carbonyl group and the aromatic ring:



Resonating structures of phenylethanone (acetophenone)

The result of this interaction is a weakening of the positive charge on the carbonyl carbon atom through dispersal of the charge into the ring.

With the above general ideas, it will be easier to understand the reactions of aldehydes and ketones. Many of the reactions given below are shown by all aldehydes and ketones, but some members show exceptional behaviour which we will take up separately.

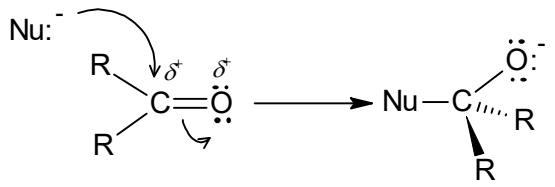
18.4.1 Nucleophilic Addition Reactions

The main reaction of aldehydes and ketones is **nucleophilic addition** to the partially positive carbon of the carbonyl group. This addition can take place by two pathways: i) nucleophilic addition-protonation and ii) electrophilic protonation or addition of other Lewis acid –nucleophilic addition. We will now take up the mechanism of both the pathways in detail.

The Mechanism of Nucleophilic Addition-Protonation

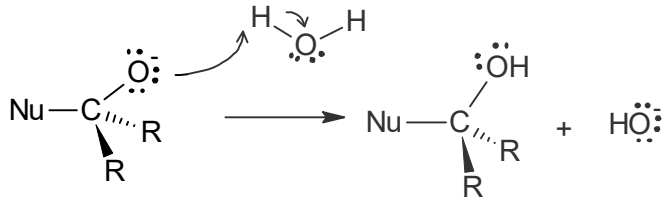
Necleophilic addition reactions in neutral or more commonly in basic condition follow the mechanism as shown below:

Step 1: Nucleophilic attack



Notice how the nucleophile approaches the electrophilic carbon and breaks the π bond of carbonyl group. This also results in rehybridisation of carbonyl carbon from sp^2 to sp^3 and the electron pair of the π bond moves over the oxygen, thereby producing an alkoxide .

Step 2: Protonation

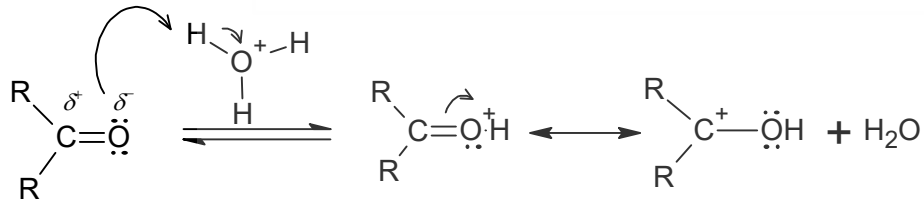


In second step, alkoxide ion abstracts a proton from protic solvents such as water or alcohol to yield the final addition product.

Protonation - Nucleophilic Addition

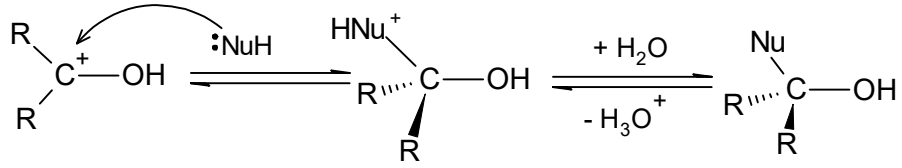
This mechanism predominates under acidic condition and begins with the attack of a electrophilic proton or other Lewis acid on nucleophilic oxygen (Lewis base) of carbonyl group. Protonation increases the electron deficiency of the carbonyl carbon and makes it more reactive toward nucleophile.

Step 1: Protonation

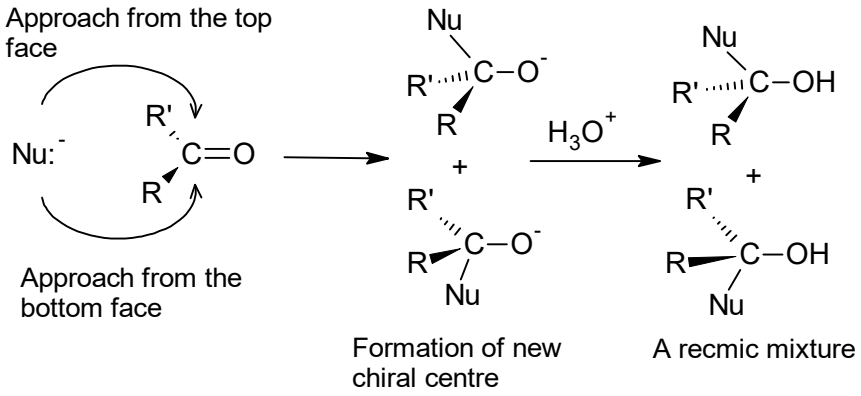


Step 2 and 3: Nucleophilic attack and deprotonation

The carbocation formed in step 1 reacts with the nucleophile, followed by loss of a proton which completes the addition process.



Weakly basic nucleophiles follow this mechanism. The acidic conditions are not suited for strong basic nucleophile. It is also important to note that in normal situation, in both the mechanisms the nucleophile can approach the carbonyl carbon from either side with equal probability. As a result, the carbonyl addition product will consist of racemic mixture if it is a chiral rectant.



But in recent past, many stereoselective neucleophilic addition reactions have been designed. The stereoslectivity of such reactions are either substrate controlled or reagent controlled or controlled by a catalyst. Details of such types of reactions will be studied in higher classes.

A wide variety of nucleophiles can attack the carbonyl group of aldehydes and ketones. We can categories the nuclephilic addition reactions on the basis of the nature of attacking atom in the following groups:

i) Addition of carbon nucleophiles

ii) Addition of oxygen nucleophiles

iii) Addition of sulphur nucleophiles

iv) Addition of nitrogen nucleophiles

v) Addition of hydrogen nucleophile

i) Addition of Carbon Nucleophiles

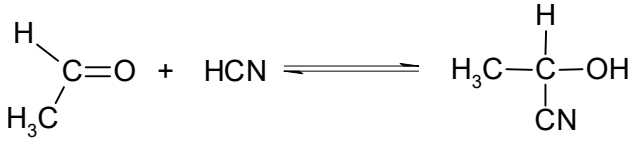
Following types of carbon nucleophiles undergo addition reaction with aldehydes and ketones:

$^{-}$:C≡N:	RC≡C:$^{-}$	RMgX	RLi
Cyanide ion	**An anion of a terminal alkyne**	**Grignard reagent**	**Organolithium reagent**

Additions of such nucleophiles have lot of significance in synthetic organic chemistry because a new carbon-carbon bond is formed in the process. These reactions are carried out in neutral conditions or basic conditions and they follow two step nucleophilic addition-protonation mechanism.

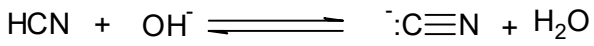
Addition of Hydrogen Cyanide

Aldehydes and ketones react with hydrogen cyanide to form nitriles (cyanohydrins), for example, HCN adds to ethanal to form 2-hyroxypropanenitrile (acetaldehyde cyanohydrin).



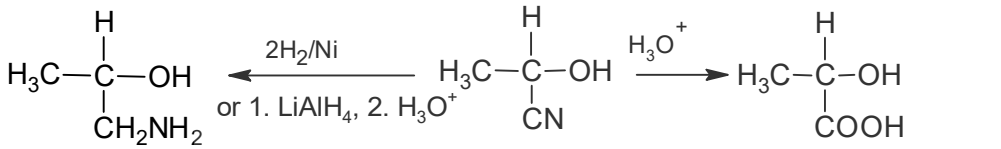
2-Hydroxypropanenitrile
75 % yield

These reactions are reversible and occur very slowly as cyanide ion is a poor electron donor (weak nucleophile), but their rates are greatly increased by the addition of alkali. This is because added alkali increases the concentration of the cyanide ion,



It is difficult to handle HCN because it is volatile nature (b.p. = 26 °C) at room temperature and is also toxic in nature. Therefore, appropriate mixture of KCN/NaCN and HCl is used in place of HCN. For aldehydes and simple ketones, the position of equilibrium favours nitrile formation. Nitrile formation is not a useful reaction for aromatic ketones and sterically hindered aliphatic ketones as the position of equilibrium for these compounds favours starting materials.

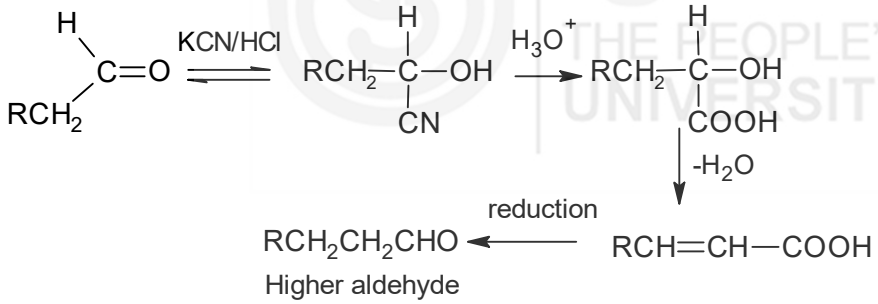
Nitriles are useful in synthesis as they can be modified by further reactions. Hydrolysis of nitriles gives α-hydroxyacids and their reduction gives primary amines:



1-Amino-2-propanol

2-Hydroxypropanoic acid

An important consequence of the hydrogen cyanide addition reaction is that one more carbon atom is added to the carbon chain. For example,



Higher aldehyde

Thus, nitriles are valuable intermediates for the synthesis of other useful organic compounds.

SAQ 5

Arrange the following carbonyl compounds in order of favourability of formation of nitriles:

Propanal, propanone, methanal and 1-phenylethanone

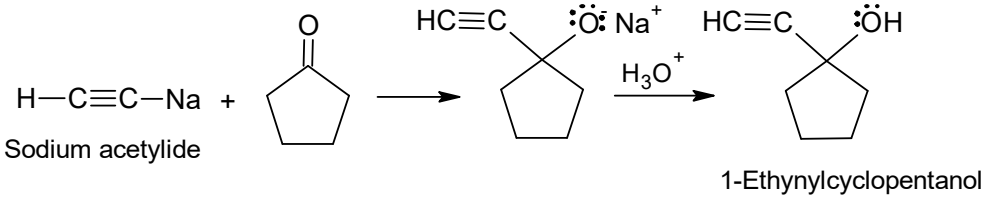
SAQ 6

How will you prepare butanal from propanal?

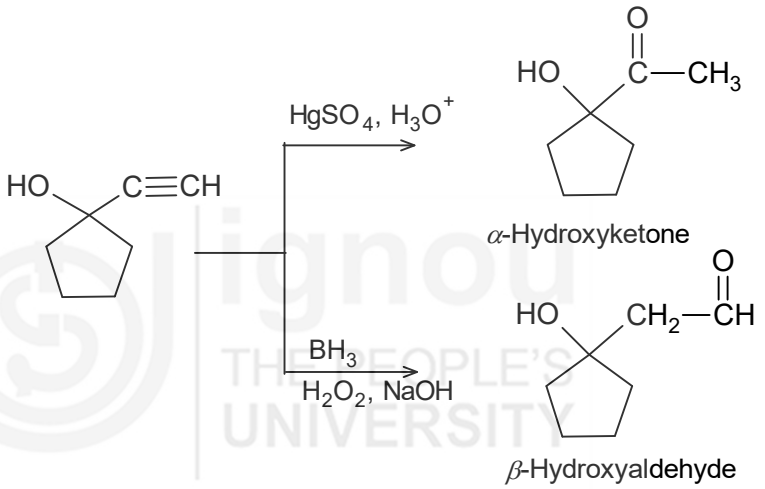
Addition of Anions of Terminal Alkynes

As discussed earlier that the hydrogen atom of a terminal alkyne is weakly acidic, and it reacts with a suitable base to generate a conjugate base, the

alkyne anion. Alkyne anions are carbanions and classified as strong nucleophiles. Alkyne ions undergo addition reactions with the carbonyl group of aldehydes and ketones. In the following example, addition of the sodium acetylide to cyclopentanone followed by hydrolysis in aqueous acid gives 1-ethynylcyclopentanol.

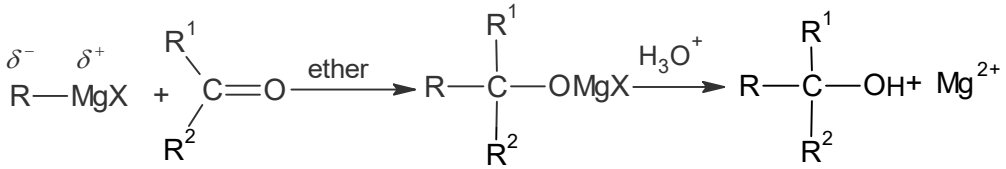


This reaction is also very useful in synthesis as both the functional groups of adduct (alkynyl alcohol) can be further modified. For example, acid catalysed hydration of 1-ethynylcyclopentanol gives an *α*-hydroxyketone and its hydroboration followed by oxidation with alkaline hydrogen peroxide gives a *β*-hydroxyaldehyde.



Addition of Grignard Reagents

The special significance of the addition of the Grignard reagents on a carbonyl group of aldehydes and ketones is that they provide excellent way to form new carbon-carbon bond. General reaction of the addition of Grignard reagent to aldehydes or ketone is that



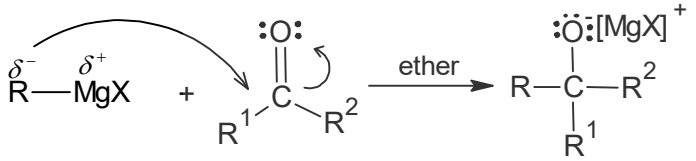
This reaction was discussed in earlier unit. As mentioned earlier, the carbon-magnesium bond of a Grignard reagent is polar in nature because of the difference in electronegativity between carbon and magnesium (2.5 – 1.2 = 1.3). In this bond, carbon bears a partial negative charge and magnesium bears a partial positive charge. Therefore, Grignard reagent is a good nucleophile and adds to carbonyl group of the aldehydes and ketones to form adduct, which on protonation in aqueous acid gives an alcohol. The reaction of Grignard reagent with methanal (formadehyde) gave primary alcohol, with other aldehydes gave secondary alcohols and with ketones gave

tertiary alcohols. Grignard reactions must be performed in dry ether. Even traces of moisture can be neutralised the reagent. Let us study the mechanism of the reaction of Grignard reagent with carbonyl compounds.

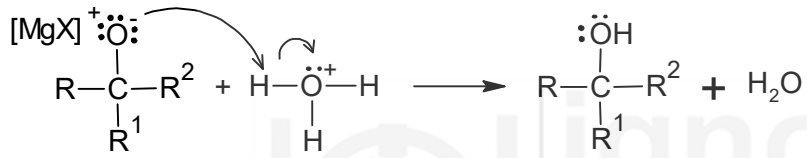
Mechanism: Reaction of Grignard reagent with aldehydes and ketones

When a Grignard reagent is mixed with an aldehyde or ketone, the negative hydrocarbon group quickly attacks the positive carbonyl carbon and provides the two electrons needed for the new carbon-carbon bond. The π electrons are displaced to the oxygen, forming alkoxoide ion in the form of alcohol salt ($-O^-[MgX]^+$. The alkoxide ion is strong base and when treated with an aqueous acid such as HCl during work up, it is protonated to form alcohol.

Step 1: New bond formation between a nucleophile and an electrophile



Step 2: Protonation

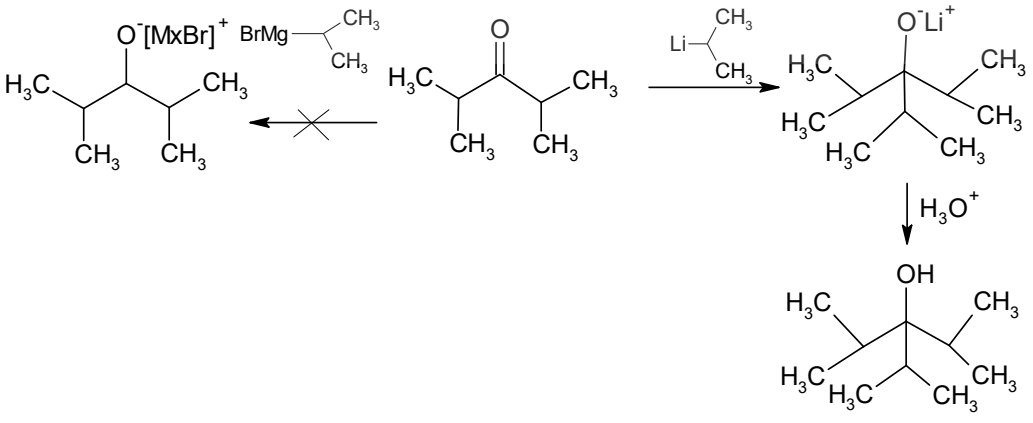


SAQ 7

How will you prepare primary, secondary and tertiary alcohols from same Grignard reagent?

Addition of Organolithium Compounds

Because of high electropositivity of lithium atom, organolithium compounds have greater negative charge on carbon. Therefore, they are generally more reactive in nucleophilic addition reactions than organomagnesium compounds. These compounds are very useful in addition reactions to sterically hindered ketones. In the following example, the Grignard reagent does not react with ketone but the organolithium does since it is stronger nucleophile.



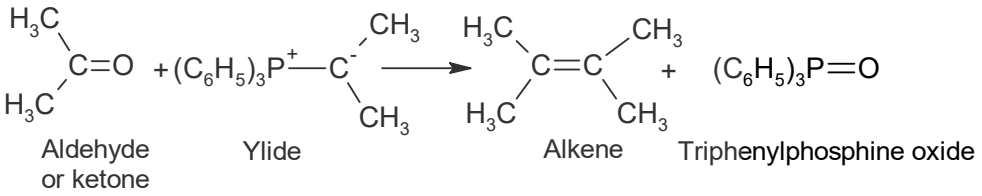
SAQ 8

Write the reaction mechanism of the following reaction:

PhCHO + BuLi → PhCH(Bu)OH

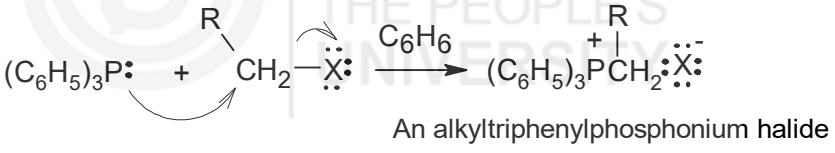
Wittig Reaction

A very important method of synthesis of alkenes known as Wittig reaction involves the reaction between an aldehyde or ketone and a phosphorus ylide. Phosphorus ylides contain a carbanion which is stabilised by an adjacent positively charged phosphorus group.

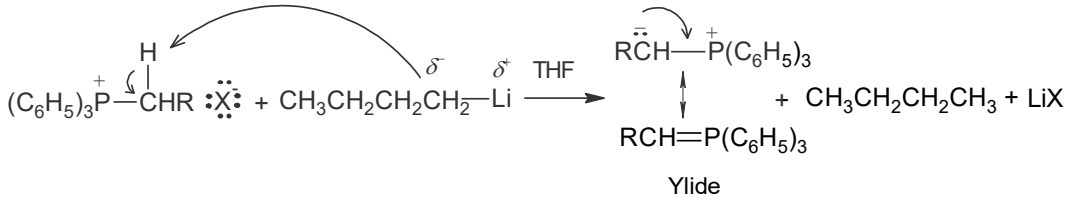


In this reaction, the oxygen of the carbonyl group is substituted by an alkene group, triphenyl phosphine oxide being the other product.

Phosphorus ylides are prepared from haloalkanes by two step sequence: the first step is the S_N2 displacement of halide by triphenylphosphine [$(C_6H_5)_3P$] to give an alkyltriphenylphosphonium salt.



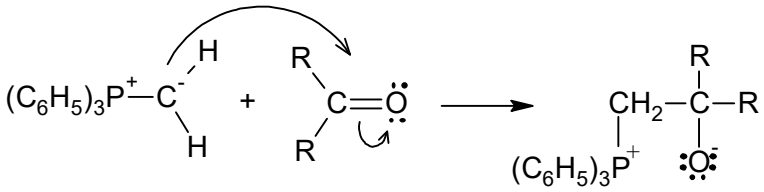
α-Hydrohen atoms on the alkyl group of an alkyltriphenylphosphonium ion now become weakly acidic in nature due to the presence of adjacent positively charged phosphorus atom and can be removed by very strong base such as butyllithium (BuLi) or sodium hydride. (NaH) to give ylide.



Mechanism

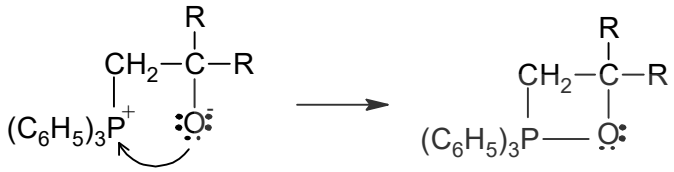
The carbanion in the ylide is nucleophilic and can attack the carbonyl group. The result is a dipolar intermediate called a betaine. The betaine is short lived and collapses to a four membered oxaphosphacyclobutane (oxaphosphetane) ring. This substance finally breaks to give alkene and triphenylphenylphosphine oxide. The driving force for the last step is the formation of very strong phosphorus-oxygen double bond.

Step 1: Bond formation between a nucleophile and an electrophile

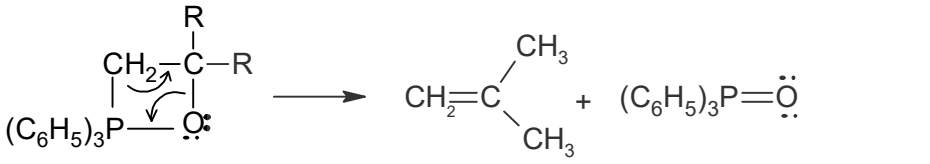


A betaine

Step 2: Formation of four membered ring



Step 3: Braking of four membered ring to more stable products

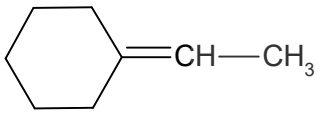


An alkene Triphenylphosphine oxide

Wittig reactions display useful steroselectivity. The reaction of non-conjugated ylides (unstabilised ylides) and aldehydes typically results in *Z* (*cis*) alkenes as major product and conjugated ylides (stabilised ylides) frequently result in trans products. Because of this, Wittig reaction is of considerable importance in industrial synthesis. Much of the synthetic vitamin A is manufactured by a reaction sequence involving Wittig reaction.

SAQ 9

Show how the following alkene can be synthesised by the Wittig reaction:

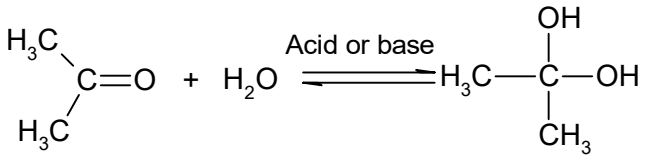


ii) Addition of Oxygen Nucleophiles

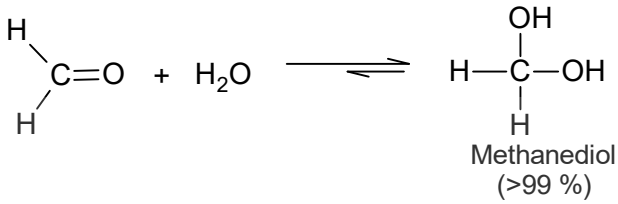
In this section, we examine nucleophilic addition reactions of aldeydes and ketones with water and alcohols. Both water and alcohols are very weak nucleophiles. Therefore, these reactions are reversible and the position of equilibrium depends on the reactivity of carbonyl group of aldehydes and ketones.

Addition of Water

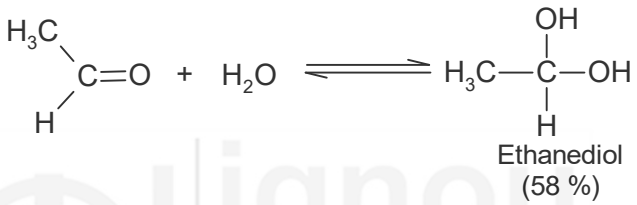
Aldehydes and ketones react with water to form 1,1-diols (Geminal diol) or hydrates. These compounds are unstable and are rarely isolated. The reaction is catalysed by acid or base. Hydration reaction is reversible and in most cases, equilibrium strongly favous the carbonyl group.

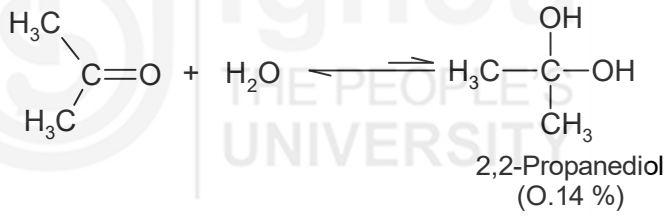


Stable hydrates are known in few cases but they are rather exceptions, For example, hydrates of 2,2,2-trichloroethanal (chloral) methanal (formaldehyde).

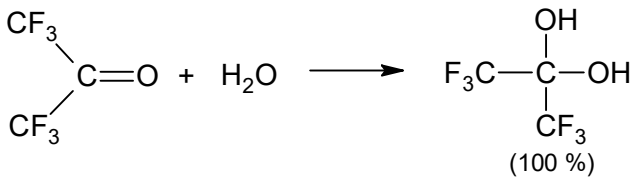


The position of equilibrium depends on the reactivity of the carbonyl group and is influenced by a combination of electronic and steric effects. With increase in size of alkyl substituent on carbonyl group, the reactivity of the carbonyl compounds decreases, For example,





As discussed earlier, the carbon atom of carbonyl group has carbocation character. Methanal has no alkyl substituent to stabilise its carbonyl group and is converted almost completely into corresponding diol. The carbonyl group of ethanal is stabilised by one alkyl substituent and carbonyl of propanone by two alkyl substituents. Thus ethanal gives 58 % of 1,2-ehanediol while propanone gives 0.15 % of 2,2-diol product. The reactivity of carbonyl group can be increased by increasing carbocation character of carbon atom of carbonyl group. This can be done by attaching electron withdrawing group to carbonyl group. For example, in contrast to almost negligible hydration of propanone, hexafluoroproanone is completely hydrated.



Above observations can also be explained on the basis of steric factor. The carbon atom that bears two hydroxyl groups is sp^3 hybridised. Its substituents are more crowded than are in the starting aldehyde or ketone. Increased crowding can be better tolerated when the substituents are hydrogen than when they are alkyl groups. Thus, diol of methanal is least crowded and hence

formed in larger amount. Diol of propanone on the other hand is more crowded, therefore, is formed in a lesser amount. The amount of diol of ethanal is formed between the above two limits. In real situation, the reactivity of aldehydes and ketones for the formation of diol depends on the combined effect of electronic and steric factors.

SAQ 10

Which of the following compounds do you predict would form hydrates and why?

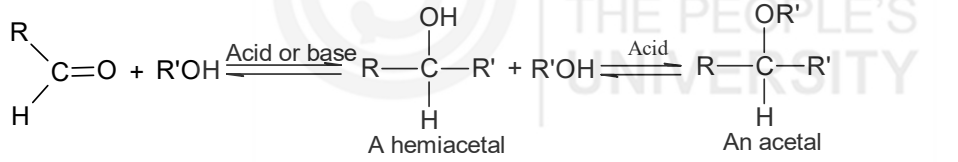
$Cl_3CCOCCl_3$, $CH_3CH_2COCH_3$

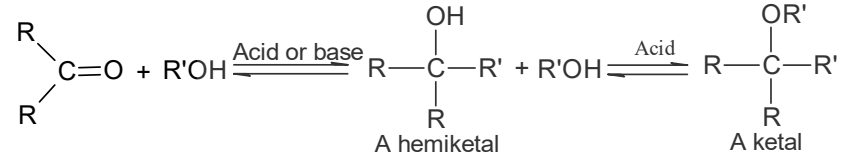
SAQ 11

Write the mechanism of both acid and base catalysed hydration reactions.

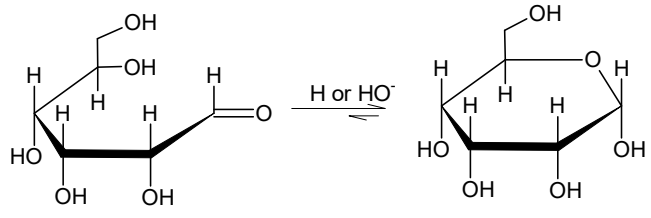
Addition of Alcohols

We have seen above that the addition reactions of water are reversible and the equilibrium is generally unfavourable. Therefore, addition reactions of water to aldehydes and ketones are generally not of much significance. On the other hand, alcohols undergo appreciable nucleophilic addition reactions to aldehydes and ketones. Let us study these reactions in some more detail. Aldehydes and ketones give first hemi-acetals (half-acetal) and hemiketals on reaction with an alcohol, respectively. With excess of alcohol, they give acetals and ketals. All these reactions are catalysed by acid or base.





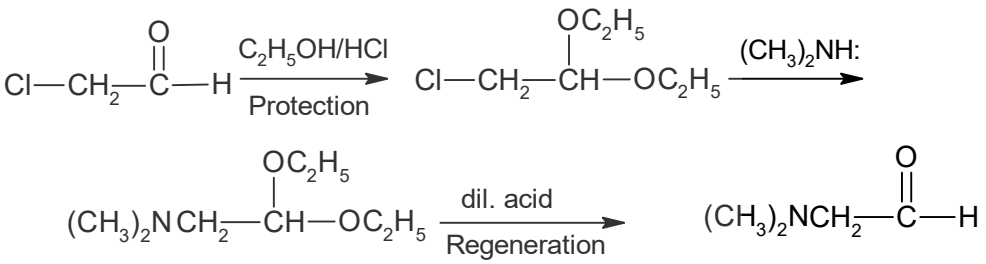
Hemiacetals are generally unstable and exist only in minor concentration in the equilibrium mixture. Exception are those from reactive carbonyl compounds such as methanal or 2,2,2-trichloroethanal.Five and six membered cyclic hemiacetals also are quite stable. Such hemiacetals are common in sugar chemistry. For example in aqueous solution, the cyclic forms constitute more than 99% of the mixture.



Aldehyde form (0.003 %)

Cyclic hemiacetal (two stereoisomers) (90 %)

Hemiacetals are generally not stable relative to starting materials, but they react further with alcohols to form acetals. Acetals are more stable than hemiacetals and can be isolated in good yield under the proper conditions. Like other ethers, acetals are good solvents. They are stable to bases and oxidising agents, but are cleaved even by dilute acids. The mechanism of cleavage reaction is just the reverse of that for the formation of the acetals. This property of acetals is used in synthesis to protect the carbonyl function from reacting while a substitution or addition reactions is carried out elsewhere in the molecule. After the reaction the acetal is then hydrolysed back to the aldehyde. The example below illustrates the utility of such protection in synthetic reactions,

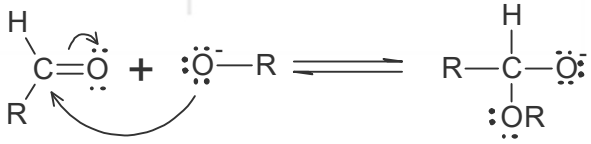


Let's study the mechanism of base-catalysed and acid-catalysed formation of a hemiacetal.

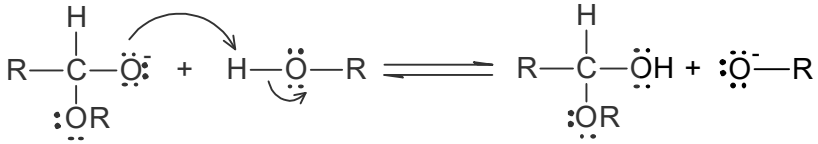
Mechanism: Base catalysed formation of hemiacetals

Step1: Alkoxide ion is formed by the proton transfer from ROH to the base.

Step 2: Nucleophilic attack on the elctrophilic carbon of carbonyl group.

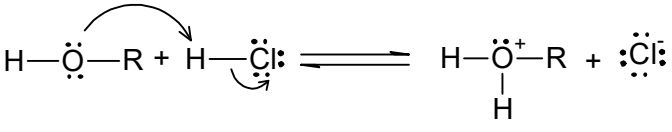


Step 3: Protonation of above addition compound.

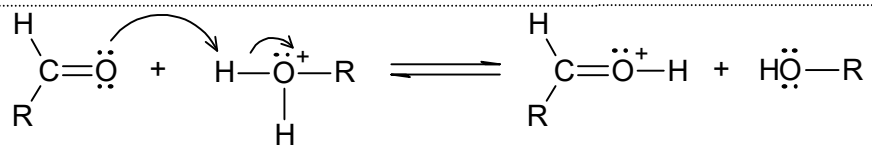


Mechanism: Acid Catalysed formation of hemiacetals

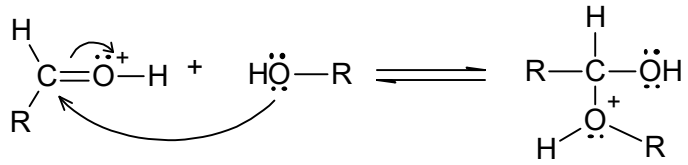
Step 1: In presence of strong acids such as HCl or sulphuric acid, alcohol molecules get protonated and this protonated alcohol will act as proton source in next step.



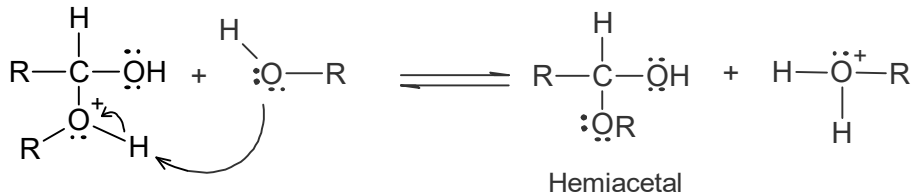
Step 2: Proton from protonated alcohol is transferred to the oxygen of carbonyl group.



Step 3: Attack of a nucleophile (alcohol molecule) to the protonated carbonyl group.



Step 4: Transfer of proton from oxonium ion to an alcohol molecule.



Hemiacetal

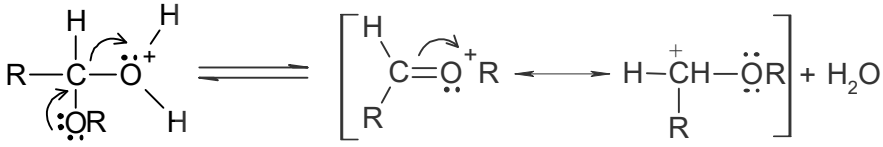
Formation of acetal from hemiacetal is catalysed by acid, not by base as it is difficult to displace, poor leaving group like −OH directly by a nucleophile. The mechanism of this reaction is as followed.

Mechanism: Acid catalysed formation of an Acetal

Step 1: Protonation of hydroxyl group of hemiacetal to form oxonium ion.

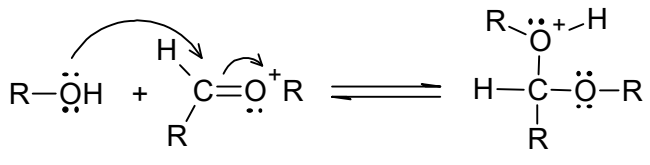
Hemiacetal An oxonium ion

Step 2: Loss of water molecule to form resonance stabilised carbocation.



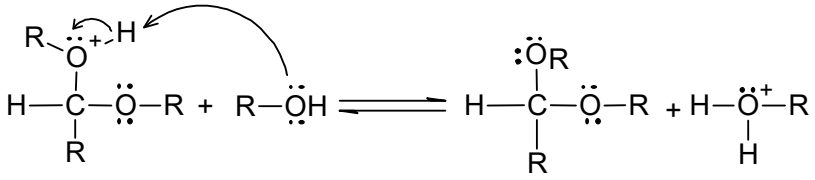
A resonance stabilised carbocation

Step 3: Nucleophilic attack on positively charged carbon atom of the carbonyl group to form protonated acetal.



A protonated acetal

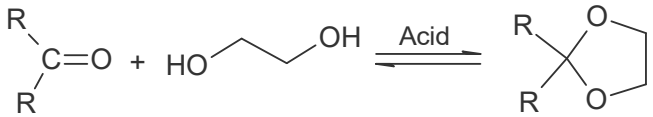
Step 4: Proton transfer from protonated acetal to alcohol molecule.



An acetal

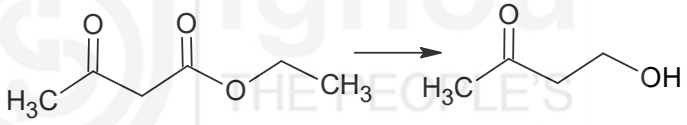
It is much more difficult to obtain ketals from ketones, as in most of cases the equilibrium favour reactants rather than products. In such situation, formation of acetal/ketal is favoured by the removing one of products, water from reaction mixture using special distillation technique.

Notice that acetal/ketal formation requires one mole of aldehyde or ketone and two moles of the alcohol. Alternatively, alcohols having two hydroxyl groups can be used in equimolar ratio to prepare cyclic acetals/ketals. Cyclic acetals or ketals are often used for protecting carbonyl group because they are easy to prepare. Sulphuric acid and *p*-toluinesulphonic acid (TsOH) are commonly used acids for the preparation of hemiacetal/hemiketals and acetals/ketals.



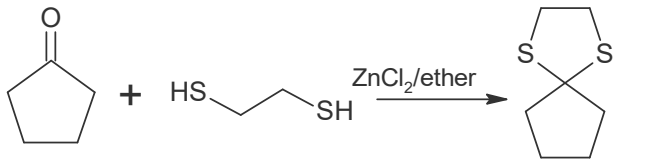
SAQ 12

How will you accomplish the following conversion?



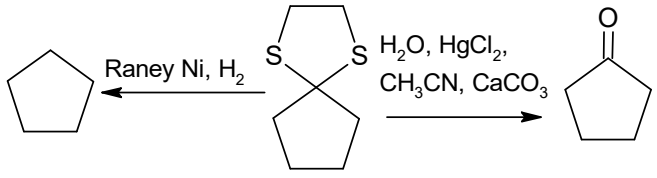
iii) Addition of Sulphur Nucleophiles

Thiols and sulphur analogs of alcohols react with aldehydes and ketones by the mechanism identical with the one discussed above for alcohols. These reactions can be catalysed by Lewis acids such as BF_3 or $ZnCl_2$. Reactions are generally carried out in ether solvent. Cyclic thioacetals/thioketals are particularly easy to prepare.



Cyclic thioketal

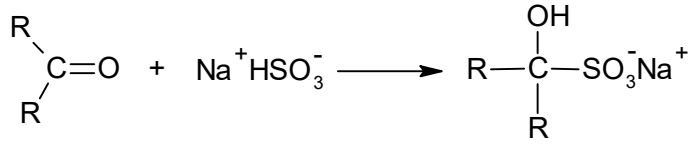
Thioacetals/thioketals are stable in aqueous acids. Their hydrolysis is carried out using mercuric chloride in aqueous acetonitrile. Thioacetals/thioketals can be desulphurised to the corresponding alkanes by the treatment with Raney nickel.



Cyclic thioacetal

Addition of sodium bisulphate ($NaHSO_3$)

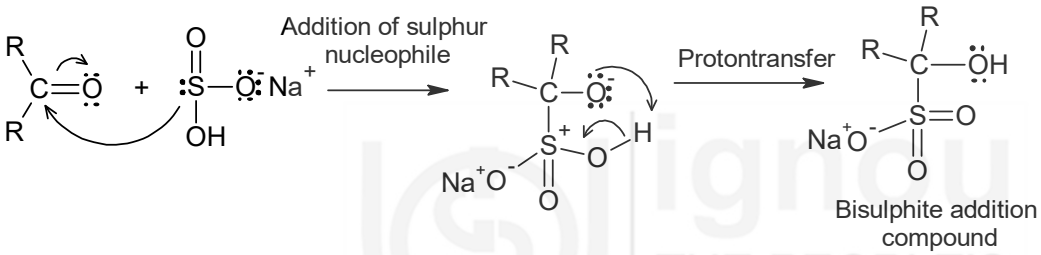
The reaction with sodium bisulphate (sodium hydrogen sulphite) gives the bisulphite adduct.



The bisulphite adducts are crystalline solids. On heating with dilute acid or aqueous sodium carbonate, they regenerate the carbonyl compound. This reaction is often used for separation and purification of aldehydes and ketones. The mechanism of this reaction is given below:

Mechanism: Formation of bisulphite a dduct

The reaction occurs by nucleophilic attack of the lone pair of sulphur on the carbonyl carbon of aldehde or ketone, just like the attack of cyanide. This leads to a positively charged sulphur atom and a simple proton transfer leads to the product.



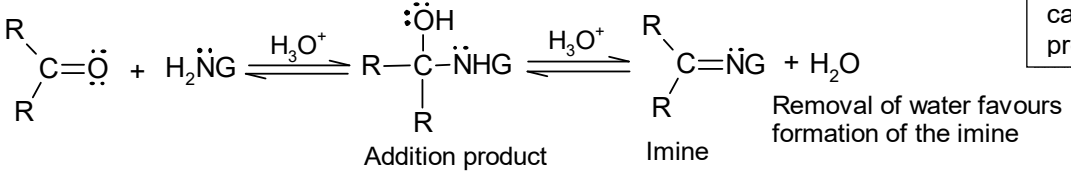
iv) Addition of Nitrogen Nucleophiles

Nitrogen nucleophiles such as ammonia and its derivatives may be regarded as nitogen analog of water and alcohols. They add to carbonyl group of aldehydes and ketones in same fashion. However, in certain cases addition products lose water, furnishing either of two new dehydrated products: imines (Schiff bases) and enamines.

Addition of Ammonia and its mono substituted derivatives (GNH_2)

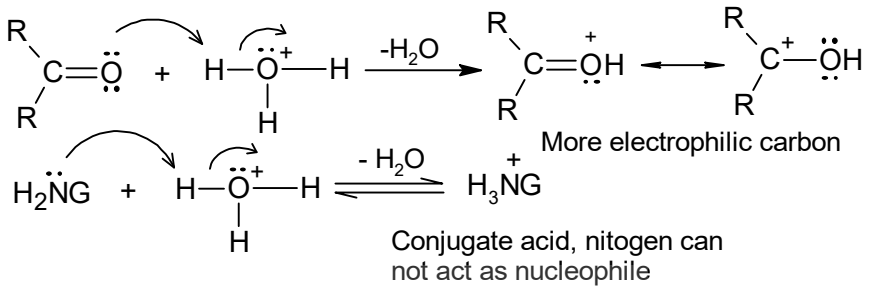
Addition of ammonia is a reversible reaction with an unfavourable equilibrium. However, certain mono substituted ammonia derivatives are added to carbonyl compounds to give imines or Schiff bases. Imine is a **condensation product** in which the initial addition is followed by dehydration to form a carbon-nitrogen double bond. The net result is substitution of oxygen by nitrogen group. Imines are generally unstable unless C=N group is part of an extended system of conjugation and are difficult to isolate from reaction mixture. The general reaction can be summed up as follows:

Organic reactions in which two molecules of starting materiel react together to form a main product plus a byproduct of considerably lower molecular mass such as H_2O or CO etc. are referred to as condensation reactions and the main product is called condensation product.



G = Groups mentioned in Table 18.5

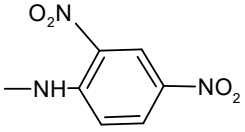
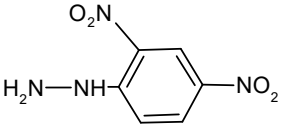
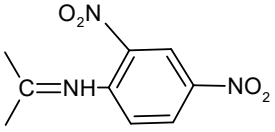
These reactions are catalyzed by acids. While protonation of carbonyl compounds increases their reactivity towards nucleophiles. But on the other hand, protonation of the reagent, H_2NG will lower its nucleophilic character as depicted below:



Therefore, an optimum pH has to be maintained during the reaction. The optimum pH for the reaction depends on the nature of G in H_2NG. It is to be adjusted such that all of H_2NG is not converted to H_3N^+G and at the same time there is sufficient concentration of the conjugate acid of the carbonyl compound to activate it.

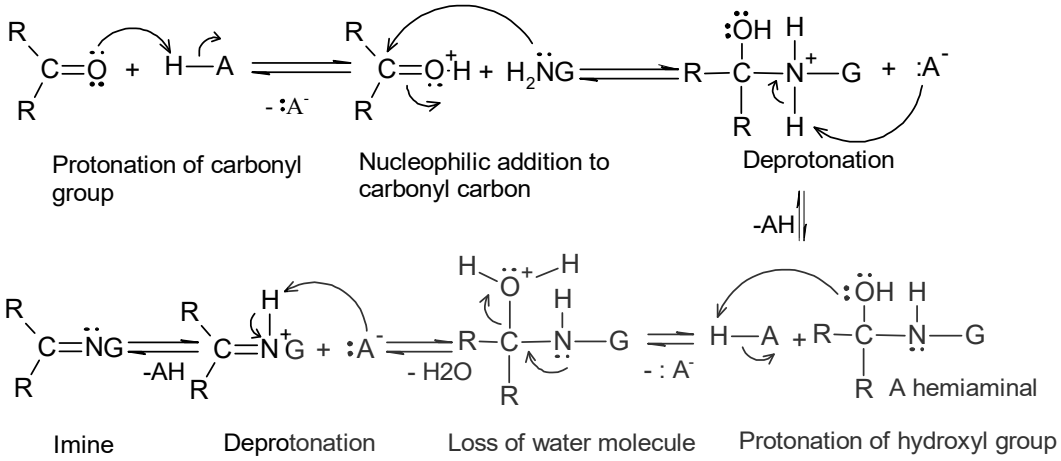
The names of reactants with different G, general condensation products and their class are given in Table 18.5. Many of these condensation products are crystalline solids with sharp melting points. For this reason they are frequently employed for the preparation of aldehyde and ketone derivatives needed for identification.

Table 18.5: Addition of ammonia derivatives

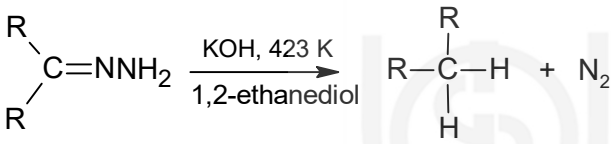
G of product	Ammonia derivative	Condensation product	Class
-R/-Ar Alkyl/aryl	RNH_2,/$ArNH_2$ Primary aliphatic amine/aromatic amine	>C = NR/.C= NAr	Imine (Schiff base)
-OH	NH_2OH Hydroxylamine	>C =NOH	Oxime
$-NH_2$	H_2NNH_2 Hydrazine	>C =NNH_2	Hydrazone
$-NHC_6H_5$	$H_2NNHC_6H_5$ Phenyl hydrazine	>C= $NNHC_6H_5$	Phenylhyrazone
$-NHNHCONH_2$	$NH_2NHCONH_2$ Semicarbazide	>C= $NNHCONH_2$	Semicarbazone
	 2,4-Diphenylhyrazine		2,4-dinitrodiphenylhyrazone

Mechanism: Formation of imine from an Aldehyde or Ketone

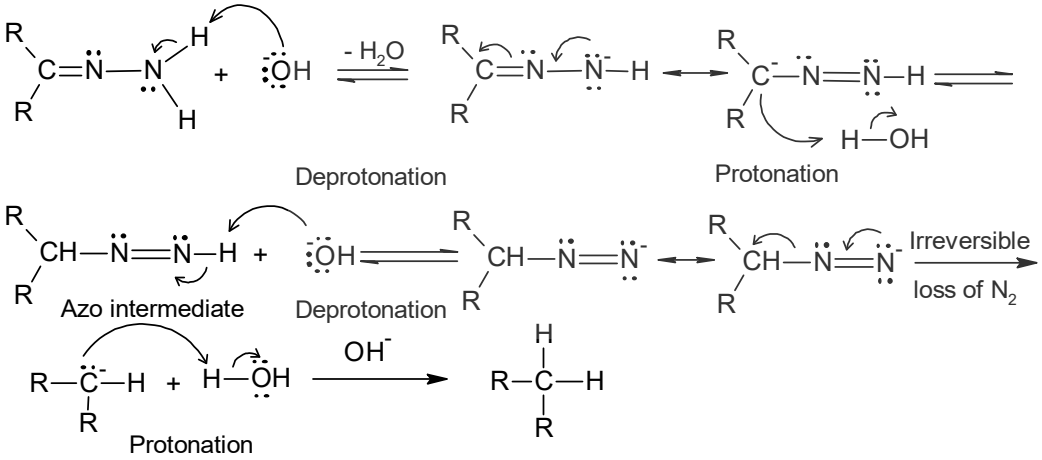
A six step mechanism for the formation of imine is shown below. The first three steps produce intermediate hemiaminal (carbinolamine) and last three steps convert this intermediate to imine.



Imines are useful compounds both in synthetic organic chemistry and in biological systems. They are used for the synthesis of complex amines. When the hydrazones are heated with potassium hydroxide or sodium ethoxide, alkanes are formed with the loss of nitrogen:



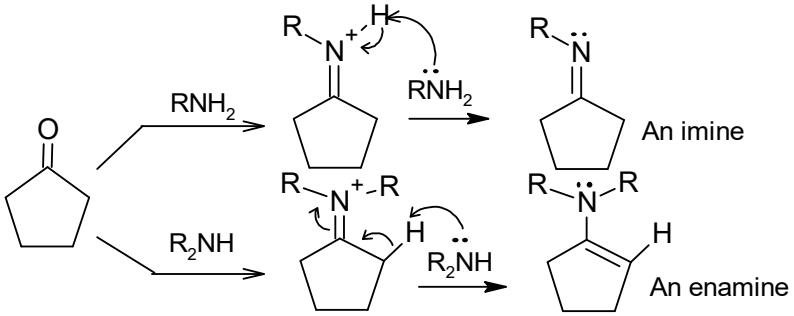
Thus the carbonyl group is converted into a methylene group via a hydrazine. This reaction is known as the **Wolff Kishner** reaction or Wolff Kishner reduction. In this reaction, base mediates hydrogen shifts. The detailed mechanism is given below.



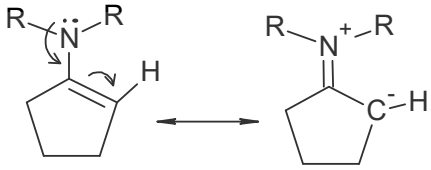
Like hydrazones, semicabozones can also be used in the above reaction.

Addition of Secondary Amines:

Secondary amines react with aldehydes and ketones to form enamines (*en* = carbon-carbon double bond, *amine* =amino group). The mechanism for the formation of an enamine is very similar to that for the formation of an imine except last step:



Enamines behave as carbon nucleophiles during organic reactions because of following resonance structures.

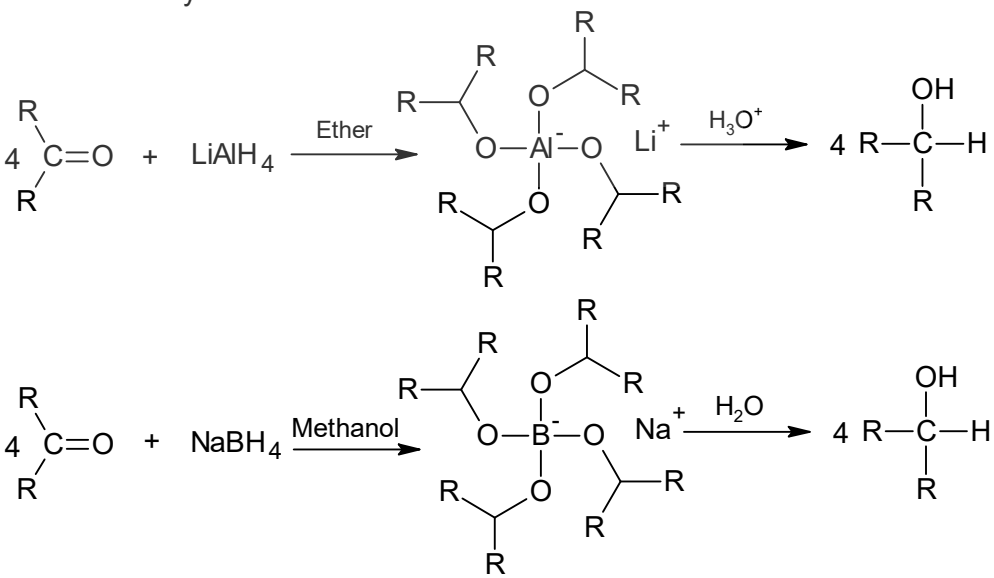


We will further go in detail of enamine chemistry and their use in synthetic organic chemistry at higher level.

v) Addition of Hydrogen Nucleophiles

Addition of hydride donors such as lithium aluminum hydride ($LiAlH_4$) or sodium borohydride ($NaBH_4$) or LiH to aldehydes and ketones gives alcohols. This addition reaction is also called a redox reaction as the reduction of a carbonyl compound to an alcohol takes place. In this unit, our discussion is only focussed on the addition reaction of lithium aluminum hydride and sodium borohydride. Both these reagents function as delivery agent of hydride (H^-).

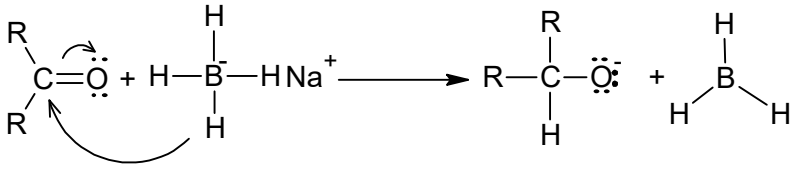
Lithium aluminum hydride is a very powerful donor of hydride. It reduces not only the carbonyl group of aldehydes and ketones rapidly but also those of carboxylic acid and their other functional derivatives. On the other hand, sodium borohydride is less reactive and, therefore a much more selective reagent, reducing only the carbonyl group of aldehydes and ketones. Because of high reactivity of lithium aluminum hydride, non protic solvents such as diethyl ether or tetrahydrofuran (THF) are used for carrying out the reaction and protic solvents such as methanol or alcohols are used for the reactions of sodium borohydride.



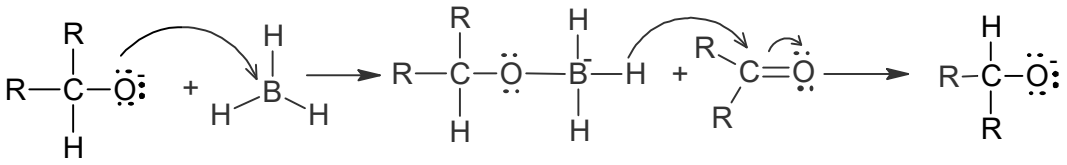
A tetraalkyl borate

Mechanism: Addition of Hydride using Sodium Borohydride

Step 1: Nucleophilic hydride ion adds to the electrophilic carbonyl carbon atom.



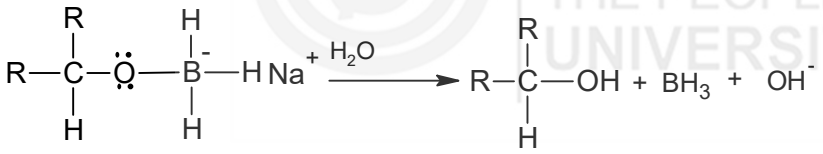
Step 2: The alkoxide ion produced in the first step can help stabilise the electron-deficient BH_3 molecule by adding to its empty *p* orbital. Now we have a tetravalent boron anion again, which could transfer a second hydride to another carbonyl group.



Second molecule of carbonyl compound

This process can continue so that, in principle, all four hydrogen atoms could be transferred to molecules of aldehyde to form tetraalkyl borate.

Step 3: Reaction is completed with the addition of proton. Water or alcohol solvent provides the proton needed to form the alcohol from the alkoxide ion.

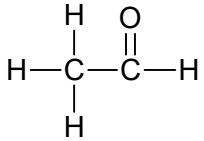


SAQ 13

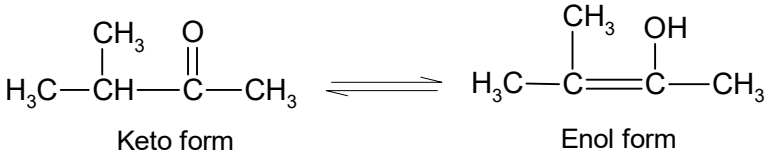
Write the mechanism for the addition of hydride to a carbonyl compound using $LiAlH_4$.

18.4.2 Reactions Involving α-Hydrogen

Another important characteristic of carbonyl compounds is the acidity of hydrogen atoms on carbon atom alpha to the carbonyl group, called α-hydrogens. We have already encountered C−H acidity in the alkynes in earlier Unit of first semester course. Propanone is about 100,000 times stronger as acid compared to ethyne. Because of the reactivity of the α-hydrogens, aldehydes and ketones may exist as equilibrium mixtures of the two isomeric forms, a keto from and an enol form.



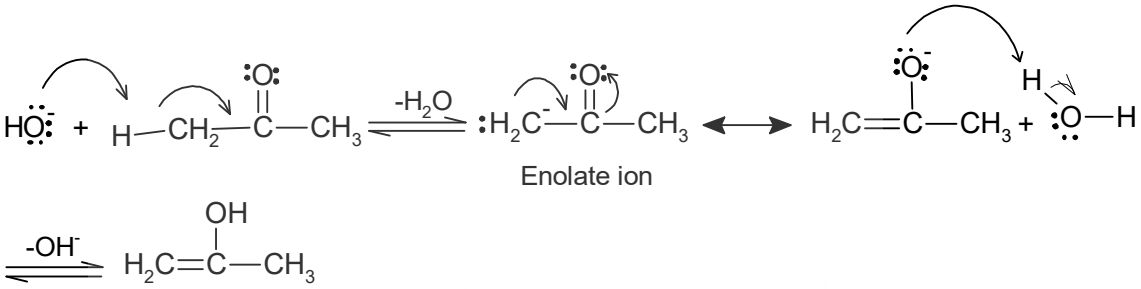
Ethanal has three α hydrogens



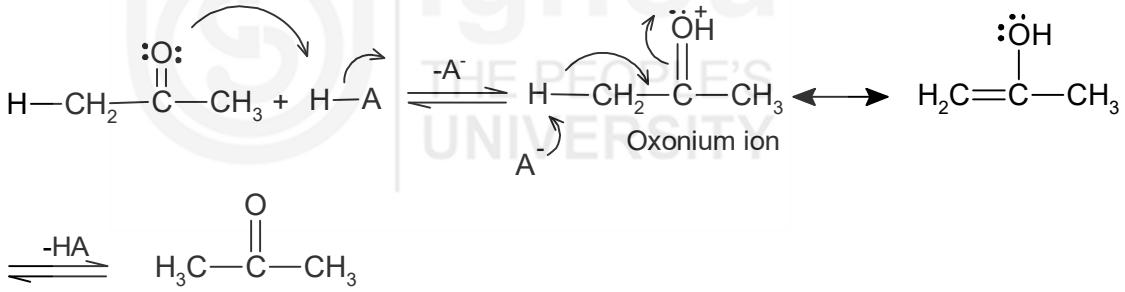
This type of isomerism in which there is dynamic equilibrium between the two forms is called tautomerism, and the isomers are called tautomers. In the pure liquid state or in neutral solutions, only traces of the enol form are present since enol form is less stable than the keto form.

Conversion of keto form to enol form is called enolisation. This conversion can be achieved by catalytic reaction with both acids and bases as shown in the following equations.

Base-catalysed enolisation



Acid-catalysed enolisation



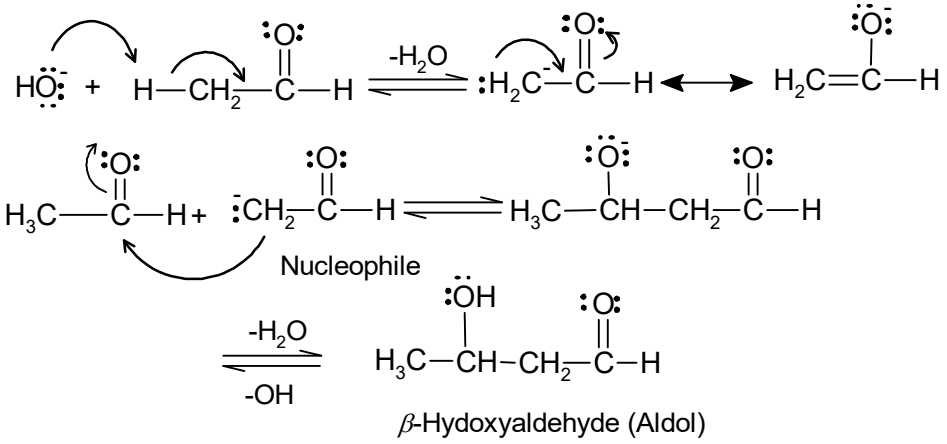
Strong acids give rise to weak conjugated bases on ionisation. The ionisation of propaone produces $^{-}CH_2COCH_3$ in which the negative change is delocalised and hence, it as a weak base. On the other hand, ionisation of CH_4 produces $^{-}CH_3$ which is a very strong base and, therefore, CH_4 is a very weak acid. The stabilisation of the anion by resonance is responsible for the greater acidity of propanone relative to methane and ethyne.

Enols and enolate ions are important reaction intermediates because they react further as nucleophiles on electrophilic carbon centres to create new carbon-carbon bonds. We will now discuss those reactions of the carbonyl compounds in which α-hydrogens are involved.

Aldol Reaction

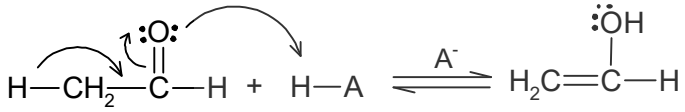
Aldol is a composite word for aldehyde + alcohol.

When an enol or enolate ion adds to another molecule of the aldehyde or the ketone, the reaction is called the **aldol**. This reaction is either base- or acid-catalysed. The mechanism of the aldol raction involving self-condensation of two molecules of ethanal in presence of a basic catalyst is shown as an example:



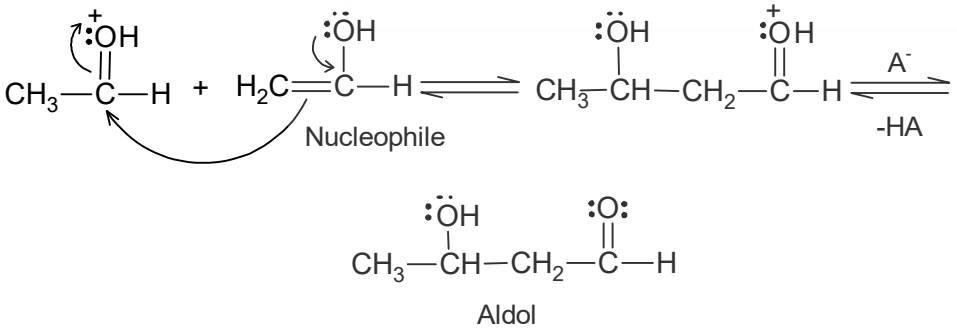
The mechanism of acid catalysed aldol reaction involves following steps;

Step 1: Acid catalysed enol formation



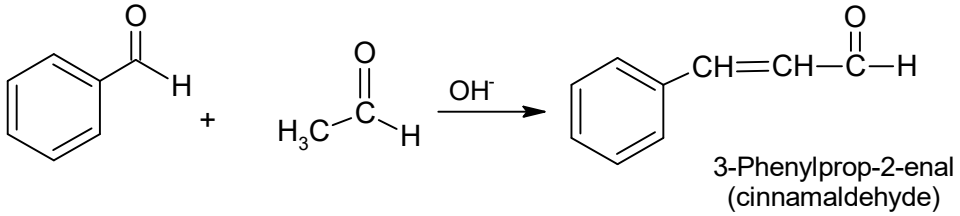
Step 2: Oxonium ion formation of second molecule of an aldehyde or a ketone.

Step 3 and 4: Nucleophilic enol attacks on electrophilc carbon atom of the oxonium ion and oxonium ion transfer its proton to conjugate base, A^- of acid HA.



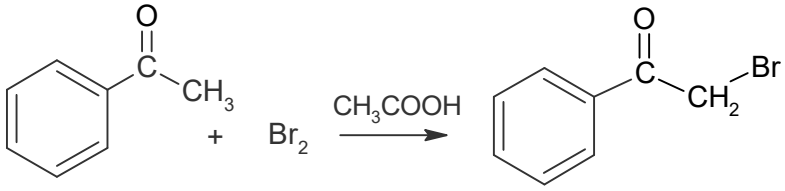
Ketones containing α-hydrogen are also capable of aldol-type of reaction. In the aldol reaction, one chiral centre is created so we expect two stereoisomers are produced as two 1:1 mixture of enantiomers. Chemists have been trying to carry out aldol and other enolate reactions in such manner that they give enantioselective products. You may study such reactions in your higher classes.

Aldehydes lacking α-hydrogens enter into a mixed aldol condensation with other aldehydes having α-hydrogens. They do this by acting as the carbanion acceptors. For example, benzaldehyde reacts with acetaldehyde to produce cinnamaldehyde, an α, β-unsaturated aromatic aldehyde used as a flavouring agent:



α-Halogenation

Aldehydes and ketones having α-hydrgen react at the α-carbon with halogens such as bromine or chlorine to form α-haloaldehydes and α-haloketones.. e.g.,



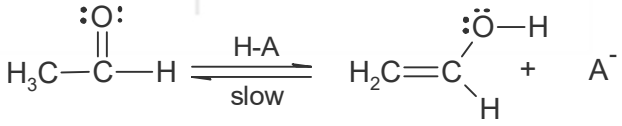
1-Phenylethanone (acetiphenone)

2-Bromo-1-Phenylethanone (α-bromoacetophenone)

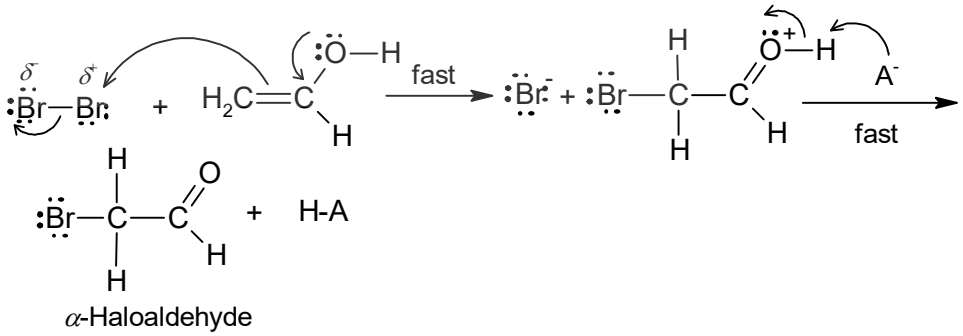
Halogenation reactions on α-carbon can be catalysed by both acid and base. Acid catalysed halogenations are generally stopped at single halogen substitution. But in the case of base catalysed halogenation, α-substituted halogen increases acidity of remaining α-hydrogens; thus, they can be removed by base with much more ease and, therefore, successive halogenations are more rapid.

Mechanism: Acid catalysed α-halogenation of an aldehde or a ketone

Step 1: Enol is formed by catalytic reaction of acid with an aldehyde or a ketone.



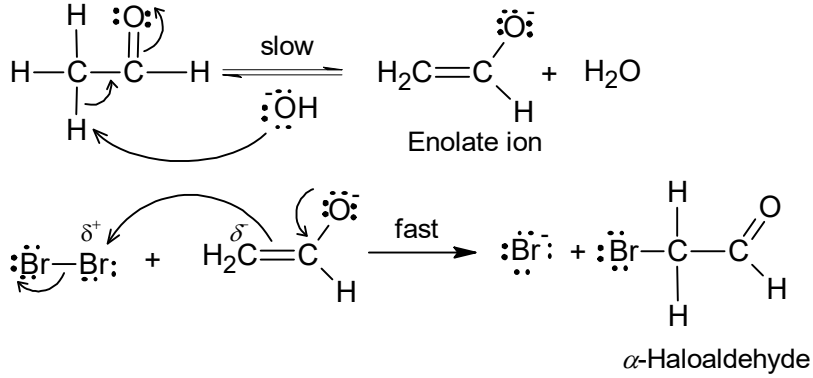
Step 2 and 3: The nucleophilic enol then attacks on electrophilic end of polarised halogen molecule and gives α-substituted intermediate which in final step transfer its proton to conjugated base of acid to gives an α-haloaldehyde or an α-haloketone.



α-Haloaldehyde

Mechanism: Base catalysed α-halogenation of an aldehyde or a ketone

In the first step, base removes an α-hydrogen from an aldehyde or a ketone to form enolate ion. In next step, this enolate ion attacks on electrophilic halogen to gives an α-haloaldehyde or an α-haloketone.

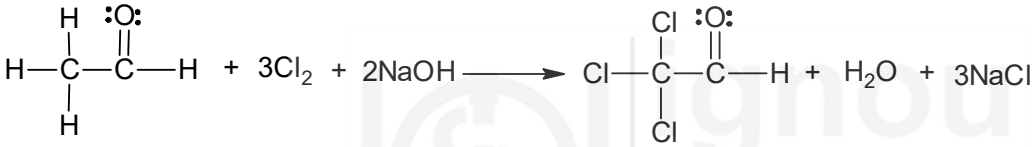


α-Haloaldehyde

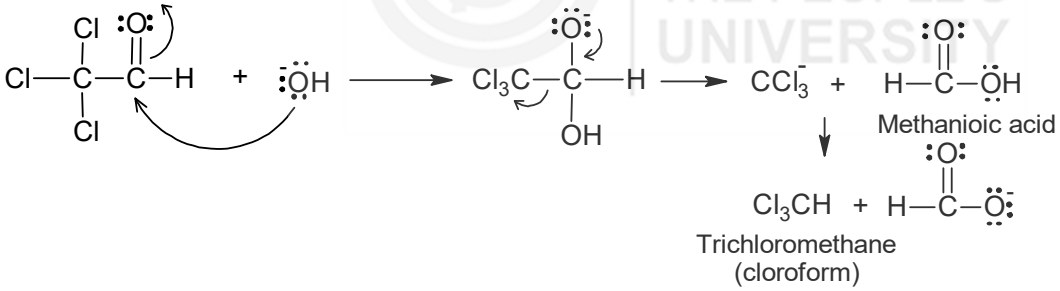
Because of high reactivity of the remaining *α* hydrogens, base catalysed halogenation tends to give polyhalogenation products. For this reason base catalysed halogenations have less synthetic use.

Furthermore, when ethanal or methyl ketones are warmed with an alkalie solution of chlorine, bromine, or iodine, the product is trichlromethane (chloroform), tribrimomethane (bromoform), or tri-iodomethane (iodoform), respectively. This reaction is called the haloform (trihalomethane) reaction and appears to take place in two stages:

Stage 1: Halogenation



Stage 2: Cleavage

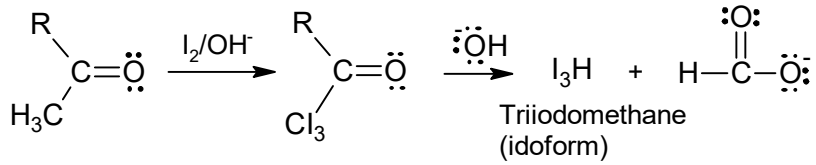


The first step is polyhalogenation *via* the enlolate ion. The second step is cleavage of the polarised Cl_3C-C bond by base through an addition elimination mechanism. The haloform reaction is useful not only as a preparartive method for the haloforms but also as a diagnostic test for the presence of the methyl ketone group or a group capable of giving methyl ketone group under the dehydrogenation. In practice, a solution of iodine is added to the aqueous alkaline solution of the compound to be tested. A positive reaction will yield tri-iodomethane (iodoform), CHI_3, a bright yellow solid which may be identified by its sharp pungent odour and its melting point. Trichloromethane and tribromomethane are liquids.

Ethanol or 2-propanol also gives idoform test as these compounds are oxidised by iodine during reaction to ethanal and propanone, respectivily.

$2CH_3CH_2OH + I_2 \rightarrow CH_3CHO + 2HI$

$2CH_3CHOHCH_3 + I_2 \rightarrow CH_3COCH_3 + 2HI$



SAQ 14

A carbonyl compound does not form iodoform on being heated with iodine and sodium hyroxide. It is:

a) ethanal

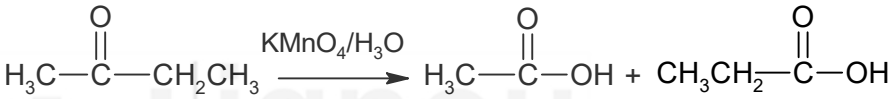
b) propanone

c) benzaldehyde

d) phenylethanone

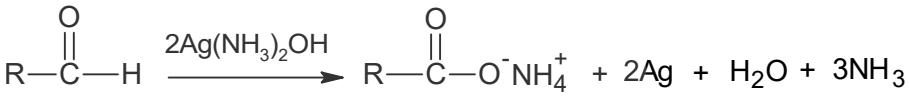
18.4.3 Oxidation

Aldehydes are oxidised so easily that even the mildest oxidising reagents will serve to bring about their conversion to acids. Ketones, on the other hand, are fairly resistant to oxidation. The oxidation of ketones, when forced by the use of strong oxidizing reagents and heat, results in the rupture of carbon-carbon bonds to produce acids.

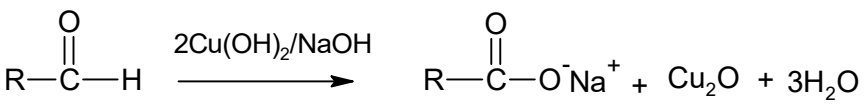


The ease with which oxidation of aldehydes takes place, provides a simple method for distinguishing between aldehydes and ketones. Mild oxidising agents may be used for this purpose. **Tollen's reagent,** an ammonical solution of silver oxide, $Ag(NH_3)_2OH$, **Fehling's solution,** an alkaline solution of cupric ion complexed with sodium potassium tartrate and **Benedicts solution,** an alkaline solution of cupric ion complexed with sodium citrate, are the three reagents commonly used to detect the presence of an aldehyde group.

When Tollen's reagent is used to oxidise an aldehyde, the silver ion is reduced to the metallic form and, if the reaction is carried out in a clean test tube, a silver mirror is formed.



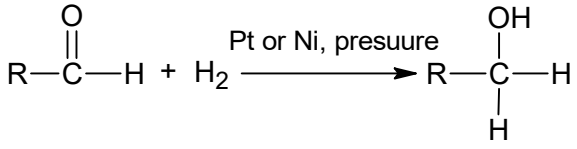
When Fehling's and Benedict's solutions are used to oxidise an aldehyde, the complexed deep blue cupric ion is reduced to red cuprous oxide.



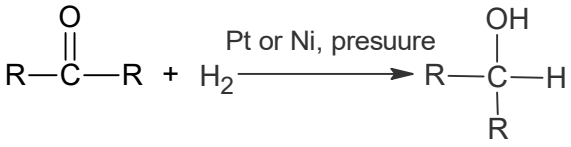
Aromatic aldehydes react with the Tollen's reagent but do not react with either Fehling's or Benedict's solution. A method of distinguishing aliphatic aldehyde from aromatic aldehydes is thus provided by this difference in reactivity between the two types of reagents.

18.4.4 Reduction

Both aldehydes and ketones undergo reduction and the nature of the product depends on the reagent used for the purpose. Catalytic hydrogenation of aldehydes and ketones gives primary and secondary alcohols, respectively. Reduction with dissolving metals (e.g., sodium-alcohol) gives alcohols similar to metallic hydrides (lithium aluminium hydride or sodium borohydride).

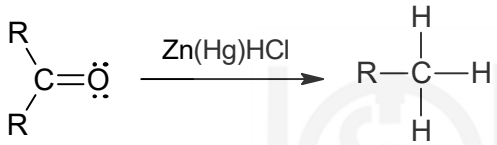


Primary alcohol

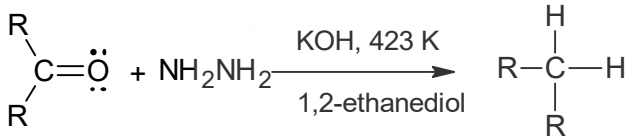


Secondary alcohol

Alkanes are formed when carbonyl compounds are reduced with zinc amalgam and hydrochloric acid. This reaction is known as the **Clemmensen reduction**.



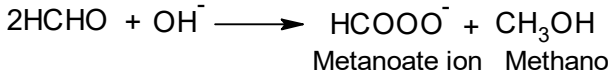
An alternative to the Clemmensen reduction for an acid sensitive ketone is the Wolff-Kishner reduction. As mentioned earlier, this employs hydrazine (NH_2NH_2) and potassium hydroxide. The solvent is 1, 2-ethanediol (glycol).



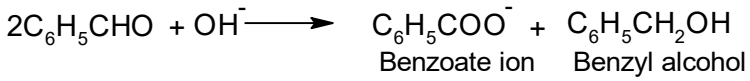
18.4.5 Specific Reactions of Aldehydes and Ketones

Methanal

Methanal (formaldehyde) gives many of the general reactions of carbonyl compounds above but as it does not have α hydrogens and therefore, it does not undergo those reactions in which α-hydrogens are involved. Thus, for example, it does not undergo base-catalysed self condensation. On treatment with aqueous sodium or potassium hydroxide it forms methanol and methanoate ion. This reaction is known as the **Cannizzaro reaction.**

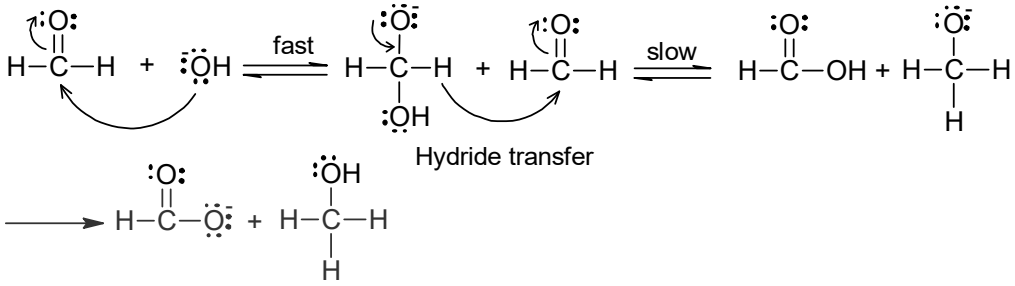


Benzaldehyde which also does not have any α-hydrogen undergoes the Cannizzaro reaction as well, e.g.,

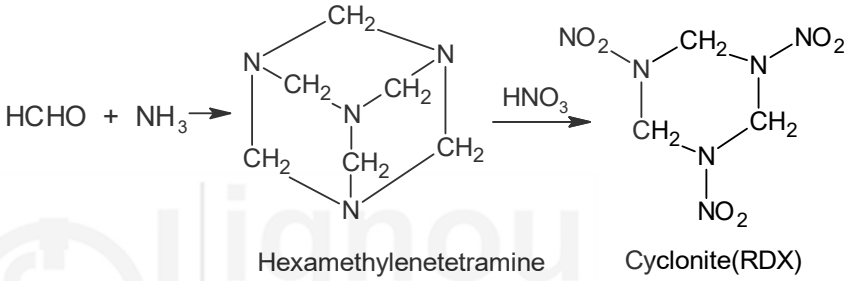


Mechanism: Cannizzaro reaction

Reaction is initiated by the addition of hydroxide ion to the carbonyl carbon to form an addition intermediate, which transfers a hydride to a second molecule of methanal in the rate determining step. After the proton transfer in final step, final product are methanol and eathanoate ion.



Treatment of methanal with ammonia gives hexamethylenetetramine: Hexamethylenetetramine is also called **urotropin** and has following cyclic structure.



Hexamethylenetetramine is medicinally useful as a urinary antiseptic (urotropine) and is also oxidized by nitric acid to the important military explosive cyclonite (RDX).

Methanal is also used as a methylating agent:

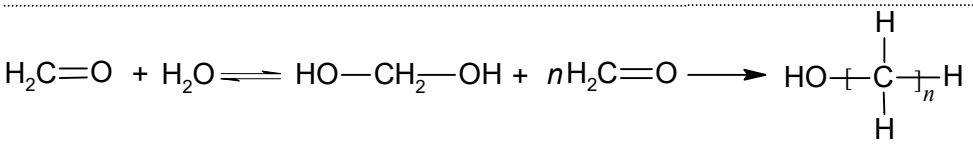
$$C_2H_5NH_2 + HCHO + HCOOH \longrightarrow C_2H_5NHCH_3 + CO_2 + H_2O$$

Aldehydes

Here we will consider reactions which are given by aldehydes only and not by ketones. Aldehydes restore the magenta colour of Schiff's reagent (aqueous rosaniline hydrochloride solution whose magenta colour has been discharged by sulphur dioxide).

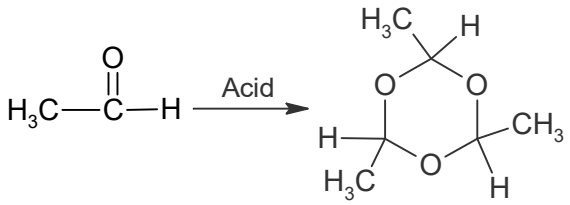
As mentioned earlier, aldehydes are very easily oxidised. Hence, they reduce Tollens' reagent to metallic silver, and Fehling's and Benedict's solutions to cuprous oxide.

Aldehydes (except methanal) on being warmed with concentrated sodium hydroxide solution, undergo aldol condensations and dehydration. Methanal and ethanal polymerise readily, propanone does not. The polymer of formaldehyde is known as **paraformaldehyde**, $HO(CH_2O)_nH$, with *n* having an average value of 30. Paraformaldehyde is an amorphous white solid which is prepared by slowly evaporating **formalin** (a 37-40% aqueous solution of methanal) under reduced pressure.



Depolymerisatin of paraformaldehyde is brought about by heating. This facile change of state from solid to gaseous allows methanal to be easily stored and used.

When treated with acid at a low temperature, ethanal undergoes addition to give a cyclic trimer, paraldehyde (b.p. 389 K). Paraldehyde, when warmed, is depolymerised to regenerate ethanal. Like methanal, ethanal can also be easily stored and is used in the form of paraldehyde.



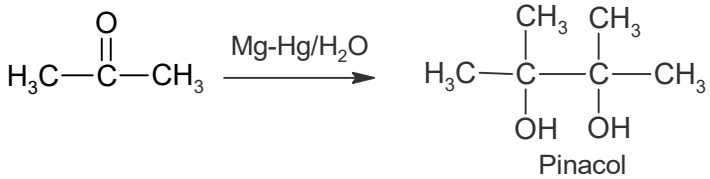
Paraldehyde

Finally in the following subsection, we will see the reactions which are given by ketones only and not by aldehydes.

Ketones

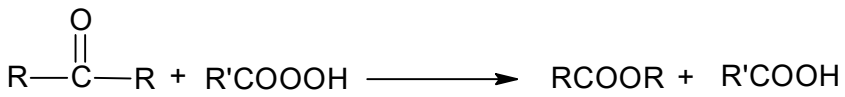
Ketones react with ammonia to give complex condensation products. Treatment with nitrous acid converts ketones to oximino derivatives, e.g.,

When reduced with magnesium amalagam and water, ketones give dimers. The dimer from propanone is called pinacol.



Pinacol

Treatment of ketones with preacids gives esters. This reaction is known as **Baeyer-Villiger oxidation**:



18.5 INDUSTRIAL USE

Methanal is perhaps the most important member of the aldehyde family. Its industrial importance lies principally in its ability to copolymerise with phenol and with urea to produce bakelite and urea methanal resins, respectively.

Methanal is also an antiseptic and disinfectant. As formalin, it is used to preserve anatomical specimens, in the manufacture of dyes, gelatin and casein.

Ethanal is used for preparing ethanol, ethanoic acid, phenolic resins, synthetic drugs and rubber accelerators. Its trimer, paraldehyde $(CH_3CHO)_3$, is used in medicine as a hypnotic.

Propanone is used as a solvent for celluloid, lacquers, cellulose acetate and nitrate and in the preparation of sulphonal and ketene ($CH_2=C=O$) for synthesis of organic compounds. Other ketones are used as solvents for resins and synthetic rubber.

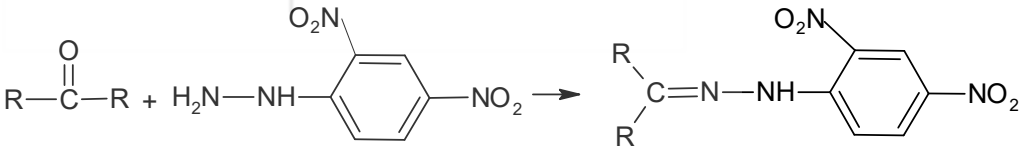
Benzaldehyde is used in perfumery, for preparation of dyes for flavouring purposes and for the preparation of α, β-unsaturated derivatives.

Phenylethanone (acetophenone) is used in perfumery and as hypnotic (hypnone). It is also used in the preparation of many organic compounds which are used in synthesis such as, phenacyl halides 1, 3-diketones, etc.

Some insecticides are prepared from the condensation of carbonyl compound, e.g., DDT (Unit 11) is obtained by heating trichloroethanal (chloral) with chlorobenzene in the presence of concentrated sulphuric acid.

18.6 LAB DETECTION

Both aldehydes and ketones on heating with an alcoholic solution of 2,4-dinitrophenyl hydrazine (DNP) in acidic medium give orange red crystalline hydrazine derivatives which are identified by their characteristic melting points.



Aldehyde or Ketone 2,4-Dinitrophenyl hydrazine 2,4-Dinitrophenyl hyrazone

Aldehydes reduce Tollens' reagent and Fehling or Benedict solutions, while ketones do not. These tests provide methods for distinguishing between aldehydes and ketones. Glucose (an aldehyde) when heated with Fehling solution gives red precipitate. This test is both qualitative as well as quantitative. It is used to estimate the amount of glucose in a sample of urine of diabetic patients. As mentioned in Section 18.4.2, ethanal and methyl ketones are characterised through the tri-iodomethane test (iodoform test).

SAQ 15

How might you use simple test tube reactions to distinguish between:

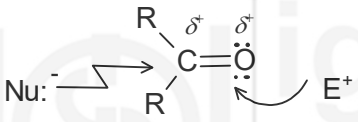
a) Benzaldehyde and ethanol

b) Ethanal and propanone

18.7 SUMMARY

In this unit, we have described the chemistry of aldehydes and ketones. We summarise below what we have studied so far:

- Aldehydes and ketones have carbonyl (> C=O) group which is quite reactive. Ketones can be regarded as alkyl or aryl derivatives of aldehydes.
- Aldehydes and ketones are prepared by oxidation or dehydrogenation of alcohols, decomposition of calcium salt of carboxylic acids or catalytic decomposition of carboxylic acids, Rosemund's method and Stephen's method.
- Methanal is commercially obtained by the catalytic oxidation of methanol. Ethanal and propanone are prepared industrially either by hydration of alkynes or catalytic oxidation of alkenes. Propanone is also obtained from oxidation of natural gas and as a by-product in the oxidation of cumene.
- The > C = O function in aldehydes and ketones undergoes addition reaction. As it has a polarized caron oxygen double bond, nucleophiles add to the carbonyl carbon atom and electrophiles add to the carbonyl oxygen atom.



Carbonyl group is attached by a variety of reagents such as HCN, $NaHSO_3$, ROH, ammonia derivatives, RMgX etc. to give addition products.

- The reaction of aldehydes and ketones with phosphorous ylildes gives alkenes (Wittig reaction). In certain aldehydes and ketones, where α-hydrogens are present, acid or base catalysed enolisation, base-catalysed halogenation, haloform reaction and aldol condensation, etc., are observed.
- Aldehydes can be oxidised to carboxylic acid; ketones cannot be oxidised without breaking carbon-carbon bonds. The carbonyl group of an aldehyde or ketone can be reduced to alcohol by either catalytic hydrogenation or metallic hydrides. They can also be reduced to alkanes by either the Wolff-Kishner or Clemmensen reduction.
- Methanal reacts with aq. NaOH to give a mixture of alcohol and carboxylate ion (Cannizzaro reaction). Methanal reacts with ammonia to form hexamethylenetetramine. Methanal and ethanal readily polymerise.
- Ketones from oximino derivatives with HNO_2, are oxidised to esters with peracids and form pinacols with magnesium amalgam water.
- Detection of carbonyl group is achieved by the formation of crystalline 2, 4-dinitrophenyl hydrazones. Aldehydes are detected by the reduction of ammoniacal silver nitrate or Fehling solution and by Schiffs' reagent.

18.8 TERMINAL QUESTIONS

1. Predict the products in the following reactions:

   a) $RCH_2OH \xrightarrow[\text{Pyridine}]{CrO_3}$

   b) $HC{\equiv}CH \xrightarrow[Hg^{2+}]{H_3O^+}$

   c) $H_3C{-}\overset{\overset{O}{\|}}{C}{-}Cl \xrightarrow{H_2/Pd(BaSO_4)}$

   d) $H_3C{-}C{\equiv}N \xrightarrow[2.\ H_2O]{1.\ SnCl_2/HCl}$

2. Write a mechanism for the reaction of:

   a) addition of methanol to propanal.

   b) addition of hydrazine to cyclohexanone.

3. Predict the products:

   a) $H_3C{-}\overset{\overset{O}{\|}}{C}{-}CH_3 + H_2NNH_2 \xrightarrow{H_3O^+}$

   b) $CH_3CH_2{-}\overset{\overset{O}{\|}}{C}{-}CH_3 + CH_2P(C_6H_5)_3 \xrightarrow{DMSO}$

   c) $CH_3CHO + Ag(NH_3)OH \longrightarrow$

   d) $H_3C{-}\overset{\overset{O}{\|}}{C}{-}CH_3 + Br_2 \xrightarrow{OH^-}$

   e) $CH_3CH_2CH_2{-}\overset{\overset{O}{\|}}{C}{-}CH_3 \xrightarrow[1,2\text{-ethanediol}]{H_2NNH_2,\ NaOH}$

   e) $H_3C{-}\overset{\overset{O}{\|}}{C}{-}CH_3 \xrightarrow{Zn(Hg),\ HCl}$

4. Show how to bring about the following conversions using Wittig reaction:

   a) acetone to 2-methyl-2-butene

   b) cyclohexanone to methylenecyclohexane

5. Write equations for the following named reactions.

   a) Oppenaur oxidation

   b) Cannizzaro reaction

   d) Aldol condensation

   e) Baeyer-Villiger oxidation

18.9 ANSWERS

Self-Assessment Questions

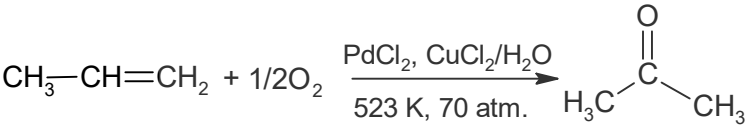
1. a) 3-methyl-3-butenal; b) cyclohaxanecarbaldehyde;

   c) cyclohexanone; d) 1-phenylbutanone

2. a) 1-pentanol; b) 3-methyl-2-butanone; c) 2-pentanol; d) cyclohexanone; e) 1-pentanal

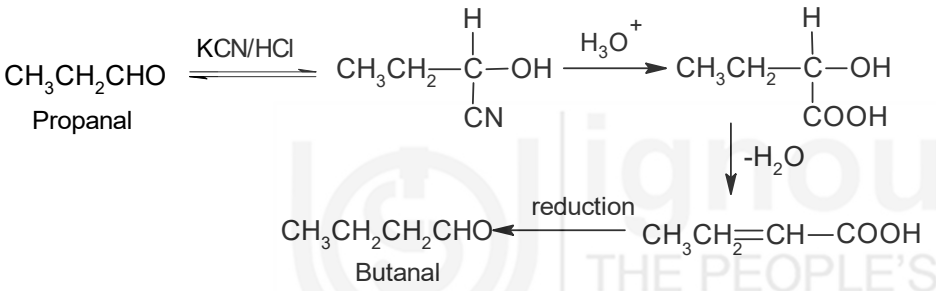
3. 2-Chloropropane

4. Propanone can be manufactured by the direct oxidation of propene from natural gas with oxygen or air, catalysed by a mixture of palladium and cuprous chlorides (**The Wacker Process**).



5. Methanal > propanal > propanone > 1-phenylethanone

6.



7. Reaction of a Grignard reagent with methanal gives primary alcohol, reaction with other aldehydes gives secondary alcohols and reaction with ketones gives tertiary alcohols.

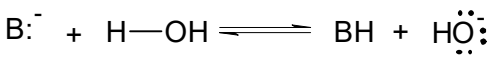
8. The mechanism will be same as for the reaction of Grignard reagent with aldehydes and ketones.

9. It can be prepared using cyclohexanone and ylide prepared from chloroethane.

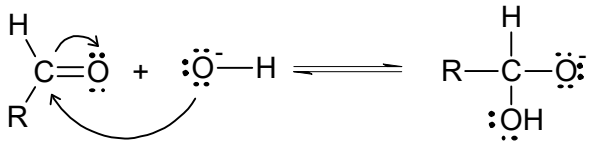
10. As discussed in text, reactivity of carbonyl group can be increases by increasing carbocation character of carbon atom of carbonyl group. $Cl_3CCOCCl_3$ has electron withdrawing group ($-CCl_3$) attached to carbonyl group. Therefore this will form hydrates.

11. Mechanism of base catalysed hydration reaction:

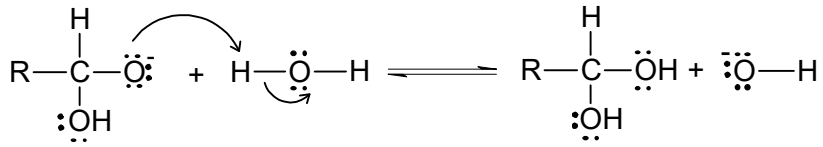
    Step 1



    Step 2

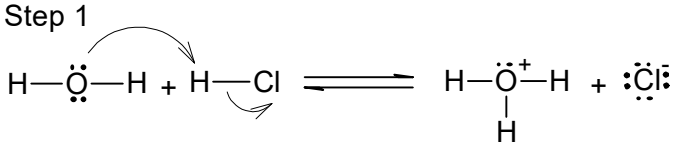


Step 3



Mechanism of Acid catalysed hydration reaction:

Step 1



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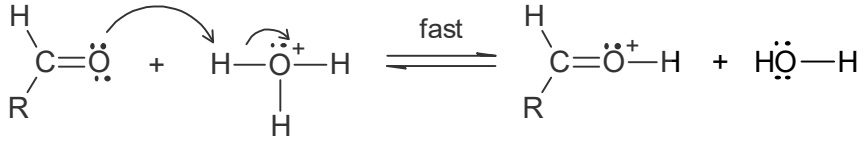

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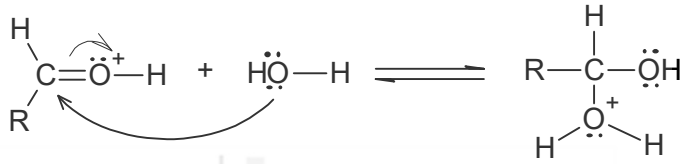
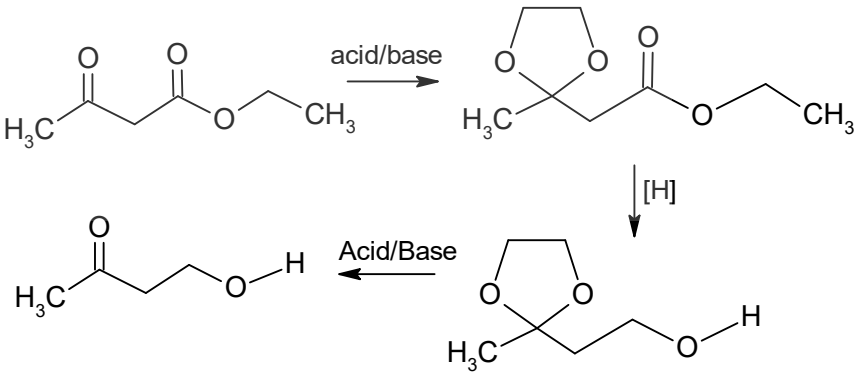
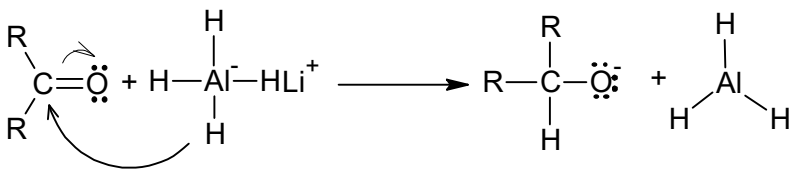


Step 4

12. First we have to protect ketone group by forming cyclic acetal, than acetal is hydrogenated to convert easter group to alcohol. Final it is treated with either base or acid back to ketone.



13. Step 1



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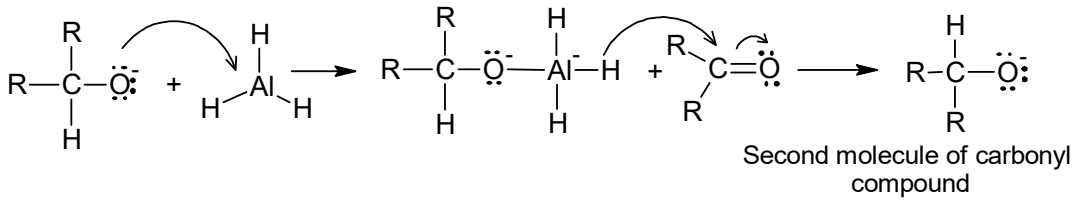
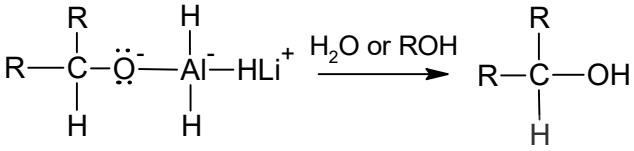


Step 3



14. c; as it is not having α-hydrogens.

15. a) Ethanal reduces both Tollen's reagent and Fehling's solution. Benzaldehyde can reduce Tollen's reagent but it does not reduce Fehling's solution. Ethanal also gives iodoform test.

    b) Ethanal reduces both Tollen's reagent and Fehling solution propanone does not.

Terminal Questions

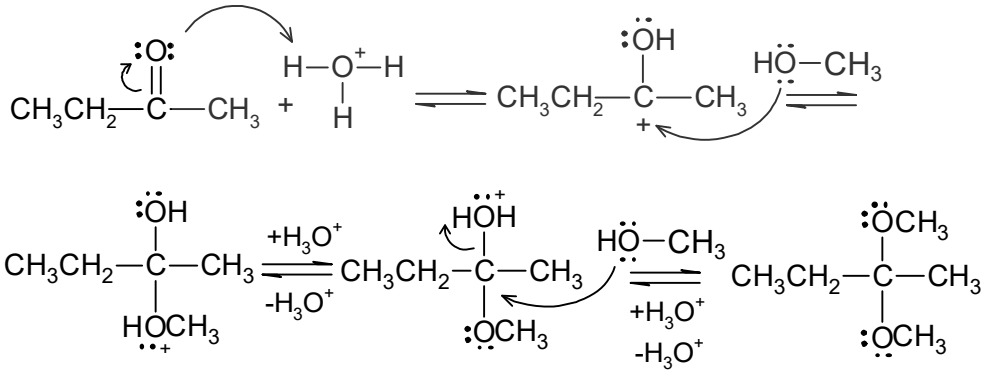
1. a) $RCH_2OH \xrightarrow[\text{Pyridine}]{CrO_3} H_3C-C(=O)-H$

   b) $HC\equiv CH \xrightarrow[Hg^{2+}]{H_3O^+} RCH_2-C(=O)-R$

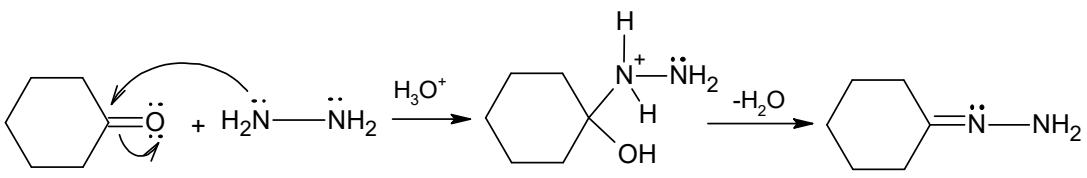
   c) $H_3C-C(=O)-Cl \xrightarrow{H_2/Pd(BaSO_4)} R-C(=O)-H$

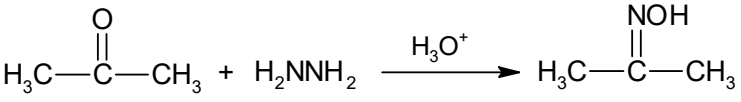
   d) $H_3C-C\equiv N \xrightarrow[2.\ H_2O]{1.\ SnCl_2/HCl} R-C(=O)-H$

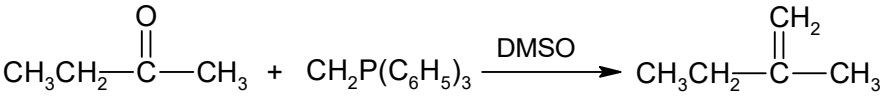
2. a)

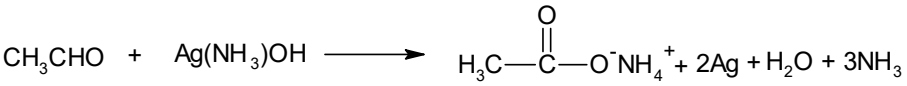


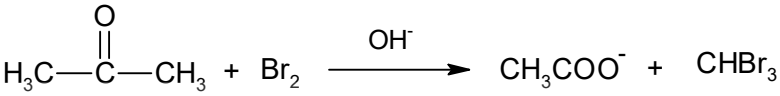
   b)

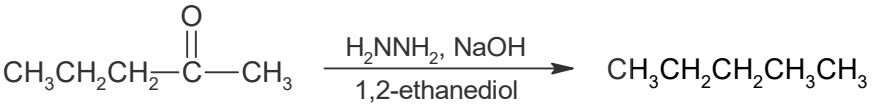


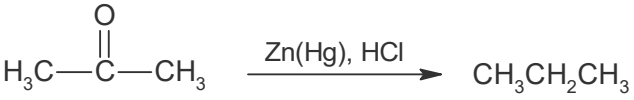
3. a) 

b) 

c) 

d) 

e) 

f) 

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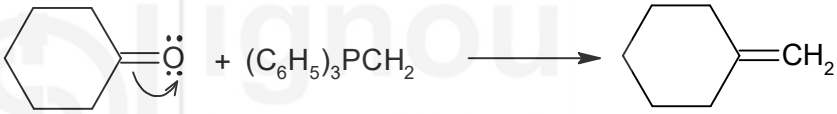
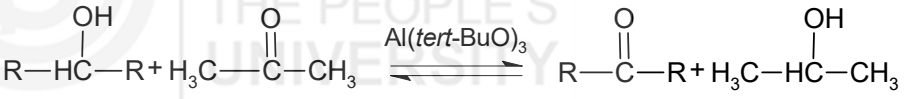
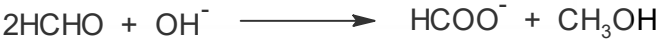
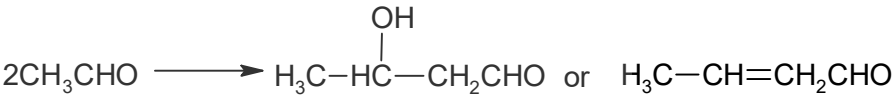
b) 

5. a) 

b) 

c) 

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